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★ ★ ★

Symposium on Treatment

Treatment—definite, specific methods of treatment as being used today in leading Boston hospitals. This is what the September number of the *Medical Clinics of North America* is bringing to its subscribers in order that they may give their patients the benefit of latest advances in office and bedside therapeutics.

For example, there will be found in this September number Clinics on the Penicillin Treatment of Staphylococci Infections, Present-day Specific Treatment of the Pneumonias, Seven Common and Important Problems in Management of Heart Diseases and Disorders, Use of Thiouracil in Treatment of Thyrotoxicosis, Treatment by the General Practitioner of Common Ear, Nose and Throat Problems, Present-day Treatment of Essential Hypertension, Functional Gastro-intestinal Disturbances, Treatment of Uncomplicated Ulcer, Disorders of Menstruation, Treatment of Chronic Diarrhea in Infancy and Childhood, etc. etc.

Year in and year out the *Medical Clinics of North America,* through such numbers as this September one, are rendering important—yes, *vital*—service to the medical profession by bringing it the new things in practice while those things are still new.

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PENICILLIN TREATMENT OF EARLY SYPHILIS: II

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In a preliminary report [1] the influence of penicillin therapy on the clinical manifestations and serologic reactions of patients with early syphilis was presented. The report was based on the results of a curtailed period of observation of a group of 4 patients. It is our purpose in the present paper to record the findings of post-treatment observation of the original group for periods in excess of three hundred days. It is also desired to record certain items of information which have resulted from the treatment of an additional 100 patients.

REVIEW OF ORIGINAL GROUP

Of the group of 4 patients the records of whom formed the basis for the preliminary report,[1] all have been maintained under observation. It will be recalled that these patients displayed dark field positive lesions of early syphilis at the time of treatment. The therapy consisted of an intramuscular injection of 25,000 units of penicillin administered at four hour intervals for forty-eight injections. The total amount of the product utilized was 1,200,000 units and the total time of therapy was about eight days. No other antisyphilitic medication has been employed. The post-treatment observation has consisted of a clinical and serologic examination at weekly intervals for the first six months and monthly observations thereafter. A spinal fluid examination was carried out at the completion of six months post-treatment observation.

Three members of the original group experienced a rapid healing of penile ulcerations and attained seronegativity within the initial three months of observation. These patients have remained clinically and serologically negative up to the present. The remaining patient has displayed circumstances which warrant discussion.

In this patient the penile lesion healed promptly and the serologic tests were recorded as negative on the 71st day. This situation maintained until the 286th day of observation, at which time strongly positive reactions were recorded in all test procedures. At that time the patient was under treatment for specific urethritis in a distant clinic. After some delay the patient was again made available for study and was found to have a single ulcerative lesion, on an indurated base, located on the inner surface of the lower lip. The regional lymph glands were enlarged and firm. There was no other evidence of involvement of skin or mucous membranes or of general adenopathy. Dark field examination of secretions secured from the lesion, after all precautions had been taken to avoid the contamination of the specimen by mouth spirochetes, was considered to be positive for Treponema pallidum.

Although this patient is being classed as a treatment failure, the probability of reinfection is inescapable. Retreatment with penicillin has been carried out.

Table 1 shows the serologic record of the first patient treated with penicillin for early syphilis. Table 2 shows the complete serologic record of patient 4, including serologic relapse or serologic upstroke accompanying reinfection.

In continuing the general study a series of approximately 100 patients have been treated in essentially the same manner as was employed in the original group. Although the post-treatment period of observation has not been of sufficient duration in a large enough group to warrant the drawing of conclusions, some interesting observations may be presented at this time. These are presented as informative material only and with the understanding that they may or may not be substantiated by more complete data.

The principal clinical features of the study may be summarized in the following manner:

The therapy has consisted of an intramuscular injection of 20,000 units of penicillin administered at three hour intervals, night and day, for sixty injections. The total amount of penicillin employed was 1,200,000 units. No other antisyphilitic medication has been used. All patients have been managed in a uniform manner, and it has not been necessary to decrease dosage or abandon the therapy in any instance. With three exceptions (acute arsenical intoxications) all the patients have displayed lesions characteristic of early syphilis (primary and/or secondary).

Herxheimer-like reactions, or therapeutic shock, of varying degrees of severity were observed during the first day of treatment in 86 patients. Ulcerations and cutaneous lesions manifested a tendency toward prompt recession. All uncomplicated ulcers were completely epithelized at the time of completion of treatment. No severe toxic reactions have been encountered. There were 2 instances of exfoliative dermatitis, 1 mild in character and of short duration, the second more severe

From the Venereal Disease Research Laboratory and the United States Marine Hospital.

Read in a panel discussion on "Penicillin in the Treatment of Syphilis" before the Section on Dermatology and Syphilology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Mahoney, J. F.; Arnold, R. C., and Harris, A.: Penicillin Treatment of Early Syphilis: A Preliminary Report, Ven. Dis. Inform. **24**: 355-357 (Dec.) 1943.

and requiring about three weeks for return to normal. The two patients had been treated with the same manufacturer's lot of material. As other irritative qualities were attributed to this particular product, the possibility of impurities being accountable for the skin reaction is present.

consideration of this phase the records of patients who have had in excess of seventy-five days satisfactory follow-up observation have been selected for scrutiny.

It may be well to state that the serologic routine which has been utilized in this study represents as complete a coverage as is practical: a total of seven

TABLE 1.—*Results of Serologic Tests in Case 1*

Duration of Disease, Nine Days

Time After Start of Therapy	Qualitative Methods: Supersensitive Kline Exclusion	Qualitative Methods: Diagnostic Flocculation: Mazzini	Qualitative Methods: Diagnostic Flocculation: Kline Diagnostic	Qualitative Methods: Diagnostic Flocculation: Kahn Standard	Qualitative Methods: Diagnostic Flocculation: Hinton	Qualitative Methods: Diagnostic Flocculation: Eagle	Qualitative Methods: Complement Fixation, Kolmer Simplified	Quantitative Methods: Diagnostic Flocculation: Mazzini	Quantitative Methods: Diagnostic Flocculation: Kahn	Quantitative Methods: Complement Fixation, Kolmer
Days										
0	..	4	..	4	Pos	Pos	4	4 4 4 2 1 -	4 4 4 2 ± -	4 4 4 4 4 1
1	..	4	..	4	Pos	Pos	4	4 4 4 2 1 -	4 4 4 2 ± -	4 4 4 4 4 3
9	4	4	4	4	Pos	Pos	4	4 4 4 4 2 -	4 4 4 4 1 -	4 4 4 4 2 -
23	..	4	..	3	Pos	Pos	4	4 3 2 - - -	4 4 1 - - -	4 4 4 3 ± -
30	4	4	3	3	Pos	—	4	4 4 4 2 - -	4 4 3 1 - -	4 4 4 2 ± -
37	4	4	1 Dbt	3	Dbt	—	3	4 4 2 1 - -	4 1 - - - -	3 3 2 ± - -
44	3	4	—	1 Dbt	—	—	4	4 3 2 - - -	4 ± - - - -	4 4 3 ± - -
51	1 Dbt	4	—	—	—	—	4	4 2 - - - -	1 - - - - -	4 4 4 1 ± -
58	1 Dbt	4	—	—	—	—	—	4 3 - - - -	1 - - - - -	- - - - - -
65	2	2 Dbt	—	—	—	—	—	2 1 - - - -	- - - - - -	- - - - - -
72	1 Dbt	2 Dbt	—	—	—	—	—	2 1 - - - -	- - - - - -	- - - - - -
80	—	2 Dbt	—	—	—	—	—	2 ± - - - -	± - - - - -	- - - - - -
86	—	2 Dbt	—	—	—	—	—	2 - - - - -	- - - - - -	- - - - - -
93	—	1 Dbt	—	—	—	—	—	1 - - - - -		
Months										
4	—	—	—	—	—	—	—			
5	—	—	—	—	—	—	—			
6	—	1 Dbt	—	—	—	—	—			
7	—	—	—	—	—	—	—			
8	—	—	—	—	—	—	—			
9	—	—	—	—	—	—	—			
11	—	1 Dbt	—	—	—	—	—			

TABLE 2.—*Results of Serologic Tests in Case 4*

Duration of Disease, Eight Days

Time After Start of Therapy	Qualitative Methods: Supersensitive Kline Exclusion	Qualitative Methods: Diagnostic Flocculation: Mazzini	Qualitative Methods: Diagnostic Flocculation: Kline Diagnostic	Qualitative Methods: Diagnostic Flocculation: Kahn Standard	Qualitative Methods: Diagnostic Flocculation: Hinton	Qualitative Methods: Diagnostic Flocculation: Eagle	Qualitative Methods: Complement Fixation, Kolmer Simplified	Quantitative Methods: Diagnostic Flocculation: Mazzini	Quantitative Methods: Diagnostic Flocculation: Kahn	Quantitative Methods: Complement Fixation, Kolmer
Days										
0	..	1 Dbt	..	—	—	—	—	- - - - - - - -	- - - - - - - -	- - - - - - - -
1	4	4	± Dbt	1 Dbt	—	Pos	—	2 1 - - - - - -	3 ± - - - - - -	± ± ± - - - - -
8	..	4	..	3	—	Pos	4	3 2 - - - - - -	4 4 ± - - - - -	4 4 4 2 ± - - -
15	4	4	1 Dbt	3	Pos	Pos	± Dbt	4 3 2 1 - - - -	4 3 1 - - - - -	± ± ± ± - - - -
22	4	3	± Dbt	3	Pos	Dbt	± Dbt	3 1 - - - - - -	4 1 ± - - - - -	± 1 ± - - - - -
30	1 Dbt	2 Dbt	± Dbt	—	Dbt	—	± Dbt	2 1 - - - - - -	1 - - - - - - -	± ± 1 ± - - - -
36	± Dbt	2 Dbt	—	—	—	—	—	2 - - - - - - -	± - - - - - - -	- - ± ± ± - - -
43	—	2 Dbt	—	—	—	—	—	2 1 - - - - - -	± - - - - - - -	- - - - - - - -
50	± Dbt	1 Dbt	—	—	—	—	—	1 - - - - - - -	- - - - - - - -	- - - - - - - -
57	—	1 Dbt	—	—	—	—	—	1 - - - - - - -	± - - - - - - -	- - - - - - - -
64	± Dbt	1 Dbt	—	—	—	—	—	1 - - - - - - -	- - - - - - - -	- - - - - - - -
71	—	—	—	—	—	—	—	- - - - - - - -	- - - - - - - -	- - - - - - - -
86	—	—	—	—	—	—	—	- - - - - - - -	- - - - - - - -	- - - - - - - -
93	—	—	—	—	—	—	—	- - - - - - - -	- - - - - - - -	- - - - - - - -
Months										
4	—	—	—	—	—	—	—			
5	—	—	—	—	—	—	—			
6	± Dbt	—	—	—	..	—	—			
7	—	1 Dbt	—	—	..	—	—			
8	—	—	—	—	..	..	—			
Days										
286	4	4	2	4	..	..	4			4 4 4 ± - - - - -
295	4	4	4	4	..	Pos	4	4 4 4 2 1 - - - -	4 4 1 ± - - - - -	4 4 4 4 1 - - - -
318	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	4 4 4 4 4 3 - - -	4 4 4 4 4 4 ± - -
326	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 3 1 -	4 4 4 4 4 4 1 - -	4 4 4 4 4 4 4 ± -

Because of the rapid disappearance of lesions the main reliance in evaluating the therapy has been placed on the serologic tests. On the reasonable assumption that the trend of the serologic reactions may be considered as an index to the progress of early syphilis in the human being, the treated patients may be placed into several rather well defined groupings. For a

accredited methods representing supersensitive and diagnostic flocculation methods, one diagnostic complement fixation technic and three methods with which the reagin content of each positive blood specimen has been quantitated.

On the basis of an arbitrary minimum of seventy-five days of satisfactory post-treatment observation, the

records of 52 patients become available for scrutiny. The average duration of observation is one hundred and thirty-five days.

Of this group of 52 patients, 6 with dark field positive lesions were in the seronegative phase of the disease at the time of treatment and passed through the observation period without positive findings being recorded.

TABLE 3.—*Results of Serologic Tests in Case 10: Pattern Considered to Be Favorable*

Duration of Disease, Twenty-One Days

Time After Start of Therapy	Qualitative Methods: Supersensitive Kline Exclusion	Qualitative Methods: Diagnostic Flocculation: Mazzini	Qualitative Methods: Diagnostic Flocculation: Kline Diagnostic	Qualitative Methods: Diagnostic Flocculation: Kahn Standard	Qualitative Methods: Diagnostic Flocculation: Hinton	Qualitative Methods: Diagnostic Flocculation: Eagle	Qualitative Methods: Complement Fixation, Kolmer Simplified	Quantitative Methods: Diagnostic Flocculation: Mazzini	Quantitative Methods: Diagnostic Flocculation: Kahn	Quantitative Methods: Complement Fixation, Kolmer
Days										
0	± Dbt	1 Dbt	—	—	Pos	—	—	1 1 1 - - - - - -	- - - - - - - - - -	- - - - - - - - -
1	1 Dbt	3	—	2	Pos	—	—	3 3 2 1 - - - - -	2 ± - - - - - - -	- - - - - - - - -
3	1 Dbt	3	—	2	Pos	Pos	3	3 3 2 1 - - - - -	2 ± - - - - - - -	3 4 4 3 2 ± - - -
8	4	4	4	4	Pos	Pos	4	4 4 3 2 2 1 - - -	4 4 2 1 ± - - - -	4 4 4 4 4 - - - -
14	4	4	4	4	Pos	Pos	4	4 4 4 3 2 - - - -	4 4 2 ± - - - - -	4 4 4 4 3 ± - - -
20	4	4	1 Dbt	4	Pos	Pos	± Dbt	4 4 3 2 1 - - - -	4 3 ± - - - - - -	± ± 1 1 - - - - -
28	2	4	± Dbt	3	Pos	—	± Dbt	4 3 2 1 1 - - - -	4 ± ± - - - - - -	± ± ± ± - - - - -
35	1 Dbt	2 Dbt	± Dbt	1 Dbt	Pos	—	—	2 2 1 1 - - - - -	3 ± - - - - - - -	- - - - - - - - -
42	± Dbt	2 Dbt	—	—	Pos	—	± Dbt	2 1 1 - - - - - -	1 - - - - - - - -	± ± - - - - - - -
48	± Dbt	—	—	—	—	—	—	- - - - - - - - -	- - - - - - - - -	- - - - - - - - -
56	± Dbt	1 Dbt	—	—	—	—	—	1 - - - - - - - -	- - - - - - - - -	- - ± ± ± - - - -
63	—	1 Dbt	—	—	—	—	—	1 - - - - - - - -	- - - - - - - - -	- - - - - - - - -
70	—	1 Dbt	—	—	—	—	—	1 - - - - - - - -	- - - - - - - - -	- - - - - - - - -
77	—	1 Dbt	—	—	—	—	—	1 - - - - - - - -	- - - - - - - - -	- - - - - - - - -
85	—	—	—	—	—	—	—	- - - - - - - - -	- - - - - - - - -	- - - - - - - - -
91	—	—	—	—	—	—	—	- - - - - - - - -	- - - - - - - - -	- - ± ± ± - - - -
Months										
4	—	—	—	—	Dbt	—	—			
5	± Dbt	—	—	—	—	—	—			
6	—	—	—	—	—	—	—			
7	—	—	—	—	—	—	—			

Pattern showing low reading reactions at the beginning of therapy, with an increase in titer during treatment and a rapid reversal to negative.

TABLE 4.—*Results of Serologic Tests in Case 35: High Titer Reactions at Onset of Therapy*

Duration of Disease, Sixty-Nine Days

Time After Start of Therapy	Qualitative Methods: Supersensitive Kline Exclusion	Qualitative Methods: Diagnostic Flocculation: Mazzini	Qualitative Methods: Diagnostic Flocculation: Kline Diagnostic	Qualitative Methods: Diagnostic Flocculation: Kahn Standard	Qualitative Methods: Diagnostic Flocculation: Hinton	Qualitative Methods: Diagnostic Flocculation: Eagle	Qualitative Methods: Complement Fixation, Kolmer Simplified	Quantitative Methods: Diagnostic Flocculation: Mazzini	Quantitative Methods: Diagnostic Flocculation: Kahn	Quantitative Methods: Complement Fixation, Kolmer
Days										
−1	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	3 4 4 4 4 4 1 - -	4 4 4 4 4 4 4 1 -
1	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	4 4 4 4 4 3 ± - -	4 4 4 4 4 4 2 ± -
8	4	4	4	4	Pos	Pos	4	4 4 4 4 4 2 1 - -	4 4 4 4 4 2 - - -	4 4 4 4 4 4 3 ± -
13	4	4	4	4	Pos	Pos	4	4 4 4 4 4 1 - - -	4 4 4 4 4 3 ± - -	4 4 4 4 4 4 2 - -
20	4	4	4	4	Pos	Pos	4	4 4 4 4 3 1 - - -	4 4 4 4 2 1 - - -	4 4 4 4 4 1 ± - -
27	4	4	4	4	..	Pos	4	4 4 4 3 ± - - - -	4 4 3 2 ± - - - -	4 4 4 4 4 1 ± - -
34	4	4	4	4	Pos	Pos	4	4 4 3 2 - - - - -	4 3 2 1 - - - - -	4 4 4 1 - - - - -
41	4	4	2	2	Pos	Pos	4	4 3 2 1 - - - - -	4 3 ± - - - - - -	4 4 4 1 - - - - -
49	4	4	4	2	Pos	Dbt	4	4 2 2 1 - - - - -	4 ± - - - - - - -	4 4 4 ± - - - - -
56	4	3	2	± Dbt	..	—	3	3 2 1 - - - - - -	4 ± - - - - - - -	3 3 1 - - - - - -
63	4	2 Dbt	1 Dbt	± Dbt	—	—	1	2 2 - - - - - - -	2 - - - - - - - -	1 ± - - - - - - -
69	3	2 Dbt	1 Dbt	—	—	—	1	2 1 - - - - - - -	1 - - - - - - - -	1 ± - - - - - - -
91	1 Dbt	1 Dbt	—	—	—	—	—			
99	2	1 Dbt	—	—	Dbt	—	—			
112	1 Dbt	1 Dbt	—	—	—	—	± Dbt			
119	1 Dbt	1 Dbt	—	—	—	—	± Dbt			
126	± Dbt	—	—	—	—	—	—			
153	± Dbt	—	—	—	—	—	—			

A representative pattern of patients with secondary syphilis. High titer reactions show a consistent and progressive trend toward reversal to negative.

The records of 25 additional patients display positive serologic reactions in some or all test methods, with a reversal to negative findings during the observation period. The average time for reversal in this group was seventy days. Thus 31 patients may be considered as having responded in a favorable manner up to the present.

In 7 patients there has been a progressive decline in the serologic titer, and although complete reversal in all tests has not been accomplished there has not been a tendency toward a return of the high titer reactions which were recorded at the time of treatment, and it is anticipated that complete reversal will be accomplished with the passage of time. However, there is no assurance of this contingency. There is the possibility that these patients eventually will be added to the favorably reacting groups.

In an additional group of 7 patients the records display an initial post-treatment trend toward seronegativity with subsequent unmistakable evidence of a return to the high titer reactions. These are considered to be instances of serologic relapse.

The remaining 7 patients have displayed serologic patterns which render difficult the making of a favorable or unfavorable classification at this time. Some pessimism is felt as to the effectiveness of the therapy in this group.

If the patients are grouped in accordance with the stage of the disease at the time of treatment, some items of potential interest become discernible. Of the 52 patients 30 may be classed as having dark field positive primary syphilis. Of this number 1 patient, previously mentioned, developed a clinical relapse nine months following treatment. A second patient displayed a well defined serorelapse after an initial favorable serologic trend for one hundred and twelve days after treatment. An additional member of the group experienced a clinical relapse after eighty-four days of practically unchanged high titer positive serologic reactions. Two patients who have displayed a progressive but protracted trend toward reversal cannot be readily classified at this time. The remaining 25 patients are at this time clinically and serologically negative. Therefore there is a possibility of there being twenty-seven satisfactory responses.

Of the 22 patients who displayed evidence of secondary syphilis and who were well into the seropositive phase of the disease at the time of treatment, 11 have progressed to seronegativity or have displayed a consistently satisfactory trend in that direction. Four patients have shown a distinct tendency toward a recurrence of high titer reactions and must be classed as serologic relapses or as treatment failures. Two additional patients are looked on as probable failures and 5 are displaying a serologic trend which, although

TABLE 5.—*Results of Serologic Tests in Case 8: Relapse Following Initial Favorable Trend*

Duration of Disease, Forty-Six Days

Time After Start of Therapy	Qualitative Methods: Supersensitive Kline Exclusion	Qualitative Methods: Diagnostic Flocculation: Mazzini	Qualitative Methods: Diagnostic Flocculation: Kline Diagnostic	Qualitative Methods: Diagnostic Flocculation: Kahn Standard	Qualitative Methods: Diagnostic Flocculation: Hinton	Qualitative Methods: Diagnostic Flocculation: Eagle	Qualitative Methods: Complement Fixation, Kolmer Simplified	Quantitative Methods: Diagnostic Flocculation: Mazzini	Quantitative Methods: Diagnostic Flocculation: Kahn	Quantitative Methods: Complement Fixation, Kolmer
Days										
0	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 3 - -	4 4 4 4 4 4 4 ± -	4 4 4 4 4 4 4 - -
1	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 3 1 -	4 4 4 4 4 4 3 ± -	4 4 4 4 4 4 4 ± -
8	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 3 - -	4 4 4 4 4 4 1 - -	4 4 4 4 4 4 4 3 -
12	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	4 4 4 4 4 4 1 - -	4 4 4 4 4 4 1 - -
19	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 - - -	4 4 4 4 4 2 ± - -	4 4 4 4 4 4 2 - -
26	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 - - -	4 4 4 4 2 ± - - -	4 4 4 4 4 3 ± - -
33	4	4	4	4	Dbt	Pos	4	4 4 4 4 4 1 - - -	4 4 4 1 ± - - - -	4 4 4 4 4 ± - - -
40	4	4	4	4	Dbt	Pos	4	4 4 4 4 3 1 - - -	4 4 2 1 - - - - -	4 4 4 4 3 ± - - -
47	4	4	4	4	Dbt	Dbt	4	4 4 4 3 - - - - -	4 4 3 ± - - - - -	4 4 1 ± - - - - -
54	4	3	2	3	Dbt	—	4	3 2 2 2 - - - - -	4 3 1 ± - - - - -	4 4 4 3 1 - - - -
61	4	4	3	3	Dbt	—	4	4 4 4 3 2 - - - -	4 2 ± - - - - - -	4 4 4 4 4 ± - - -
68	4	4	4	3	Pos	—	4	4 4 4 3 2 - - - -	4 2 ± - - - - - -	4 4 4 4 2 ± - - -
75	4	4	4	4	Pos	Pos	4	4 4 4 4 2 - - - -	4 4 4 3 ± - - - -	4 4 4 4 2 ± - - -
82	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	4 4 4 4 4 1 - - -	4 4 4 4 4 ± - - -
90	4	4	4	4	Pos	Pos	4	4 4 4 4 4 2 1 - -	4 4 4 4 2 - - - -	4 4 4 4 4 4 ± - -
96	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	4 4 4 4 4 2 - - -	4 4 4 4 4 4 4 4 3
105	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	4 4 4 4 4 2 - - -	4 4 4 4 4 4 - - -
110	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 - - -	4 4 4 4 4 4 ± - -	4 4 4 4 4 4 ± - -
117	4	4	4	4	Pos	Pos	4	4 4 4 4 4 - - - -	4 4 4 4 4 - - - -	4 4 4 4 4 - - - -
124	4	4	4	4	Pos	Pos	4	4 4 4 4 4 1 - - -	4 4 4 3 1 - - - -	4 4 4 4 4 3 - - -
131	4	4	4	4	Pos	Pos	4	4 4 4 4 3 - - - -	4 4 4 2 ± - - - -	4 4 4 4 2 ± - - -
138	4	4	4	4	Pos	Pos	4	4 4 4 4 1 - - - -	4 4 4 4 2 - - - -	4 4 4 4 4 4 1 - -
152	4	4	3	4	Pos	Pos	4	4 2 1 - - - - - -	4 4 3 - - - - - -	4 4 3 ± - - - - -
166	4	2 Dbt	1 Dbt	3	Pos	Pos	4	.....	.....	4 4 1 ± - - - - -
188	4	2 Dbt	4	± Dbt	Pos	Dbt	± Dbt	.....	.....	± ± - - - - - - -
194	4	4	2	—	Dbt	Dbt	4	.....	.....	4 3 - - - - - - -
201	4	4	2	2	Pos	Dbt	4	4 3 2 2 - - - - -	.....	4 3 2 ± - - - - -
208	4	4	3	3	Pos	Pos	4	4 4 3 2 - - - - -	.....	4 4 4 3 ± - - - -

TABLE 6.—*Results of Serologic Tests in Case 68*

Duration of Disease, Thirty Days

Time After Start of Therapy	Qualitative Methods: Supersensitive Kline Exclusion	Qualitative Methods: Diagnostic Flocculation: Mazzini	Qualitative Methods: Diagnostic Flocculation: Kline Diagnostic	Qualitative Methods: Diagnostic Flocculation: Kahn Standard	Qualitative Methods: Diagnostic Flocculation: Hinton	Qualitative Methods: Diagnostic Flocculation: Eagle	Qualitative Methods: Complement Fixation, Kolmer Simplified	Quantitative Methods: Diagnostic Flocculation: Mazzini	Quantitative Methods: Diagnostic Flocculation: Kahn	Quantitative Methods: Complement Fixation, Kolmer
Days										
0	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 3 1 -	± ± 2 4 2 1 ± - -	4 4 4 4 4 4 4 ± -
1	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	2 4 4 4 4 2 - - -	4 4 4 4 4 4 4 ± -
7	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 1 -	2 2 2 2 2 2 ± - -	4 4 4 4 4 4 ± - -
11	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	2 4 4 4 4 1 ± - -	4 4 4 4 4 4 4 ± -
18	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	± 4 4 3 2 ± - - -	4 4 4 4 4 4 ± - -
25	4	4	2	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	2 4 4 4 3 - - - -	4 4 4 4 4 4 4 ± -
32	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	4 4 4 4 4 3 1 - -	4 4 4 4 4 4 3 ± -
39	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	2 4 4 4 4 3 ± - -	4 4 4 4 4 4 4 4 ±
46	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	2 4 4 4 2 ± - - -	4 4 4 4 4 4 4 4 ±
53	4	4	4	4	Pos	Pos	4	4 4 4 4 2 1 - - -	± ± ± 1 1 ± ± - -	4 4 4 4 4 4 3 - -
60	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 2 - -	4 4 4 4 2 ± - - -	4 4 4 4 4 4 3 - -
66	4	4	4	4	Pos	Pos	4	4 4 4 4 3 2 1 - -	3 4 4 4 3 ± - - -	4 4 4 4 4 4 ± - -
74	4	4	4	4	Pos	Pos	4	4 4 4 4 4 4 2 - -	3 3 4 4 4 ± - - -	4 4 4 4 4 4 - - -
86	4	4	4	4	Dbt	Pos	4	4 4 4 3 2 - - - -	4 4 4 ± - - - - -	4 4 4 4 4 1 - - -
93	4	4	4	4	..	Pos	4	4 4 4 4 4 3 1 - -	4 4 4 4 3 ± - - -	4 4 4 4 4 4 ± - -
109	4	4	4	4	Pos	Pos	4	4 4 4 4 4 3 1 - -	4 4 4 4 4 2 - - -	4 4 4 4 4 4 4 ± -

Pattern displayed by patient with early syphilis in which the therapy failed to influence the serologic picture.

favorable at the moment, displays a protracted decline which presages an unfavorable outcome.

The remaining tables represent serologic patterns which are considered to be representative of groups of patients.

COMMENT

The contrast which is displayed in the groups of treated patients rather indicates that (1) very early infections respond in the most favorable manner and (2) the increase in probable failures in patients with secondary syphilis indicates the need of a more vigorous therapy than that used in this study.

In evaluating the effectiveness of arsenic therapy in syphilis and of sulfonamide therapy in gonorrhea, it has been noted that a certain proportion of individuals fail to experience the same curative response which may be demonstrable in the majority of patients. A similar characteristic seems to be emerging in penicillin therapy of syphilis.

A majority of patients with early syphilis appear to respond to treatment in a satisfactory manner, as judged by the clinical course and the trend of the serologic reactions. A small group in the present series (7 definitely and 2 probably) appear to have derived a minimum of permanent benefit and must be considered as treatment failures.

In sulfonamide therapy of gonorrhea, failures of this type are classed as sulfonamide resistant and much has been written in regard to the drug resistance of strains of Neisseria gonorrhoeae. While accepting as possible that strain characteristics may play a role in determining the effectiveness of a therapy, it is felt that certain host factors are largely responsible for determining whether or not an agent, as penicillin, will be effective in infections which are amenable, as a rule, to treatment. It is felt that one of the most important problems in chemotherapy is a delineation of this essential factor and the development of means through which it may be favorably influenced.

In all the patients who have been classed as failures an observation period in excess of eighty-four days was required before an adverse decision as to treatment status was considered warranted. The data in these instances and in those which may occur among patients treated in the future will be scrutinized in an effort to determine a reliable basis for a more prompt decision predicated on clinical response and serologic pattern.

The making available of a pure or reasonably pure penicillin might effect a distinct change in the treatment picture both as to results produced and as to the duration of treatment, dosage and the interval between injections. Equally important will be the development of an assay method which gives assurance that the spirocheticidal activity of a product is consistently proportional to the antibacterial activity on which the present Oxford unit is based.

CONCLUSION

It is desired to recall that the disease syphilis is one which is characterized by chronicity, with long periods of latency and a distinct tendency to clinical and serologic recurrence. The evaluation of any therapy will require a prolonged trial utilizing a wide variety of treatment schedules and a carefully controlled follow-up system. The combined experience available at this time has served to illuminate only a few of the important aspects. The remainder must await the passage of time.

THE TREATMENT OF EARLY SYPHILIS WITH PENICILLIN

A PRELIMINARY REPORT OF 1,418 CASES

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In December 1943 Mahoney, Arnold and Harris [1] reported briefly on the effect of pencillin in experimental syphilis of rabbits and in 4 human patients with seropositive primary syphilis. As a result of these observations and of further experimental studies carried out in the laboratories of Mahoney [2] and Eagle [3] there was organized, about Sept. 1, 1943, under the general auspices of the Committee on Medical Research of the Office of Scientific Research and Development and under the specific direction of the Subcommittee on Venereal Diseases, National Research Council, a cooperative study of the effect of penicillin in syphilis in human beings. A Penicillin Panel was appointed by this subcommittee, with membership including the authors of this paper.[4] Because of the special problems confronting the armed forces, particular emphasis has been laid on early syphilis and on neurosyphilis, though other forms of late syphilis have also been studied. The preliminary results obtained to date are here presented in two papers; this dealing with early syphilis; the other, with Stokes as spokesman for the group, with late syphilis.

The penicillin employed has been derived from Army, Navy, Public Health Service, and Office of Scientific Research and Development sources. Only the sodium salt has been employed in these studies. Penicillin allocated to the Office of Scientific Research and Development for research purposes has been distributed by the Committee on Chemotherapeutic and Other Agents, National Research Council, Dr. Chester Keefer, chairman. This committee has allocated gradually increasing amounts of the drug to the Subcommittee on Venereal Diseases, which in turn has apportioned it among those civilian clinics selected for participation in the study.

Early syphilis is at present under investigation in twenty-three clinics or research centers. These, with the names of the responsible investigators, are as follows: U. S. Army (Fort Bragg, North Carolina, Capt. William Leifer, Camp Howze, Texas, Major Franklin Grauer), U. S. Navy (Naval Medical Center, Bethesda, Md., Lieut. Comdr. E. C. Barksdale), United

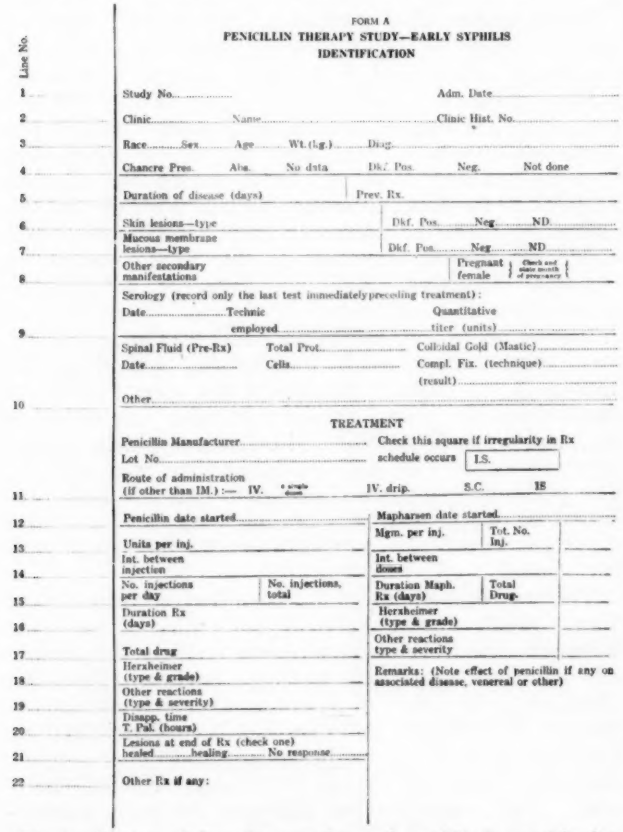
The authors are members of the Penicillin Panel of the Subcommittee on Venereal Diseases, National Research Council.

The work described in this paper was done under several contracts recommended by the Committee on Medical Research of the Office of Scientific Research and Development.

Read in a panel discussion on "Penicillin in the Treatment of Syphilis" before the Section on Dermatology and Syphilology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Mahoney, J. F.; Arnold, D. C., and Harris, A.: Penicillin Treatment of Early Syphilis: A Preliminary Report, Ven. Dis. Inform. **24**: 355, 1943.
2. Mahoney, J. F., and others: Unpublished data.
3. Eagle, H.: Unpublished data.
4. Dr. J. R. Heller Jr., medical director in charge Venereal Disease Division, United States Public Health Service, was later added to the membership of the panel.

States Public Health Service (Marine Hospital, Stapleton, S. I., Dr. J. F. Mahoney), Massachusetts Memorial Hospital, Boston (Dr. Oscar Cox), Bellevue Hospital, New York (Dr. Evan Thomas), Chicago Intensive Treatment Center (Dr. S. W. Becker), Cleveland City Hospital and University Hospitals (Dr. Harold Cole), University of Pennsylvania Hospital (Dr. J. H. Stokes), University of Texas (Dr. Chester Frazier), Washington University, St. Louis (Dr. W. Barry Wood Jr.), Yale University (Dr. Francis Blake), Dallas Venereal Disease Clinic (Dr. Arthur Schoch), Leland Stanford Jr. University Hospital (Dr. C. W. Barnett), Duke University Hospital (Dr. C. L. Calloway), Vanderbilt University Hospital (Dr. R. H. Kampmeier), Johns Hopkins Hospital (Drs. J. E.



FORM A

PENICILLIN THERAPY STUDY—EARLY SYPHILIS

IDENTIFICATION

Line No.

1 Study No. ..... Adm. Date .....

2 Clinic ..... Name ..... Clinic Hist. No. .....

3 Race ..... Sex ..... Age ..... Wt. (kg.) ..... Diag. .....

4 Chancre Pres. Abs. No data Dk. Pos. Neg. Not done

5 Duration of disease (days) Prev. Rx.

6 Skin lesions—type Dkf. Pos. Neg. ND.

7 Mucous membrane lesions—type Dkf. Pos. Neg. ND.

8 Other secondary manifestations Pregnant female { Check and state month of pregnancy

Serology (record only the last test immediately preceding treatment):

9 Date ..... Technic employed ..... Quantitative titer (units) .....

Spinal Fluid (Pre-Rx) Total Prot. ..... Colloidal Gold (Mastic) .....

Date ..... Cells ..... Compl. Fix. (technique) .....

(result) .....

10 Other .....

TREATMENT

Penicillin Manufacturer ..... Check this square if irregularity in Rx schedule occurs I.S.

Lot No. .....

Route of administration (if other than IM.):— IV. single dose IV. drip. S.C. IS

11

12 Penicillin date started ..... Mapharsen date started .....

13 Units per inj. Mgm. per inj. Tot. No. Inj.

14 Int. between injection Int. between doses

15 No. injections per day No. injections, total Duration Maph. Rx (days) Total Drug

16 Duration Rx (days) Herxheimer (type & grade)

17 Total drug Other reactions type & severity

18 Herxheimer (type & grade) Remarks: (Note effect of penicillin if any on associated disease, venereal or other)

19 Other reactions (type & severity)

20 Disapp. time T. Pal. (hours)

21 Lesions at end of Rx (check one) healed ..... healing ..... No response .....

22 Other Rx if any:

Fig. 1.—Obverse of form for reporting early syphilis by participating clinics.

Moore and C. F. Mohr), Tulane University (Dr. R. V. Platou), Presbyterian Hospital, New York (Dr. A. B. Cannon), University of Virginia Hospital (Dr. D. C. Smith), New York Hospital (Dr. Walsh McDermott) and the Detroit Health Department (Dr. Loren Shaffer). This report is based on the work of these investigators and of many of their associates and assistants, too numerous to name.[5]

These clinics and centers agreed (1) to treat patients with early syphilis on assigned treatment schedules in an effort to define as promptly as possible the all important time-dose relationship and (2) to pool their results under the Penicillin Panel of the Subcommittee on Venereal Diseases. Only those patients in whom the diagnosis of early syphilis was indubitable, on the basis of actual demonstration of treponemes, were to be acceptable. All patients were to be originally examined and subsequently followed in as nearly as possible a uniform manner. The immediate results of treatment were to be reported to the Penicillin Panel on specially devised forms (figs. 1 and 2), susceptible of coding, punch carding and machine statistical analysis.

5. The statistical data have been prepared by Miss Gwendolyn Futcher.

TABLE 1.—*Four Treatment Schedules*

Duration of Treatment	Interval Between Injections	Route of Administration	Single Dose	No. of Injections	Total Dose
7½ days	3 hours	Intramuscular	1,000 units	60	60,000 units
7½ days	3 hours	Intramuscular	5,000 units	60	300,000 units
7½ days	3 hours	Intramuscular	10,000 units	60	600,000 units
7½ days	3 hours	Intramuscular	20,000 units	60	1,200,000 units

On the basis of the very preliminary studies of Mahoney and his associates, there appeared to be five variables requiring study. These were (1) the route of administration, originally chosen [1] as intramuscular for the sake of slightly delayed absorption and excretion as compared to the intravenous route; (2) the interval between injections, at first selected [1] as every three hours day and night on the basis of known data as to the rate of absorption and excretion; (3) the duration of treatment, originally arbitrarily selected as eight days; [1] (4) the total dosage, again arbitrarily selected as 1,200,000 units,[1] and (5) possible combinations of penicillin with other drugs, e. g. mapharsen.

At the outset it was decided by the Penicillin Panel to hold the first three of these variables constant; i. e., all cases were to be treated by the intramuscular route every three hours day and night to a total of sixty injections given in seven and one-half days. The first effort was to be to define the minimum effective dose so given within this time period. Four treatment schedules were accordingly drawn up (table 1).

These covered a twenty fold dosage range up to and including the original maximum arbitrarily chosen by Mahoney and his co-workers. In addition there were originally planned (but subsequently temporarily dropped) two other groups, to test the combined effect of penicillin plus mapharsen. These two groups comprised a total penicillin dosage of 60,000 and 300,000 units respectively plus a total of 320 mg. of mapharsen given in eight divided doses of 40 mg. each daily for eight days. This mapharsen dosage was deliberately selected as a relatively safe and known subcurative dose from which a high rate of relapse might be expected.

Later, as material accumulated, the variable of time was brought under study, and three additional treatment groups were established with a total dosage of penicillin of 300,000, 600,000 and 1,200,000 units respectively given in thirty intramuscular injections every three hours day and night over a four day period. The latter groups have been so recently started as not to justify consideration in this paper, which is devoted entirely to the eight day treatment schedule. The only exception to the statement lies in 25 cases treated by the intravenous route before the present organized study began; in them the dosage was variable and the duration of treatment four to eight days.

TABLE 2.—*Duration of Follow-Up from Start of Treatment in 1,418 Patients with Early Syphilis (June 1, 1944)*

Duration of Follow-Up, Weeks	No. of Patients Followed
1 to 4	671
5 to 8	307
9 to 16	327
17 to 24	107
25 to 48	6

For the purposes of this report, the books of the Penicillin Panel have been temporarily closed as of May 25, 1944. To that date there had been received 1,587 case reports of early syphilis, of which 1,418 were suitable for analysis as to various points. Of these 177 had seronegative primary, 379 seropositive primary, 698 uncomplicated and 67 complicated [6] early secondary syphilis and 97 various types of recurrent (usually previously treated) secondary syphilis. Of the patients 461 were white, 950 Negro and 7 of other races; 791 were male and 627 female, of whom 58 were pregnant at the time of treatment.

The preliminary nature of this report is indicated by table 2, in which the duration of follow-up after treatment is shown. The majority of patients have so far been observed for less than two months; only 113 of the entire number for four months or longer. This fact must be repeatedly emphasized as a matter of caution; the results here presented are subject to major revision after further observation. It is planned to report further information as it develops at three to six month intervals.

THE IMMEDIATE RESULTS OF TREATMENT

Disappearance Time of Treponema Pallidum from Open Lesions.—Data are available on this point from 663 cases treated with penicillin alone (excluding those cases treated with penicillin plus mapharsen).

Regardless of the single or total dose of penicillin, organisms have promptly disappeared from open lesions in every case within a range of six to sixty hours. At the two extremes of dosage, 1,000 and 40,000 units, the average disappearance time varied only from twenty-one to fourteen hours. Whether the apparent trend toward shortening of disappearance time is significant is open to question because of the varying intervals at which dark field examinations were done in the several clinics. Not shown in the table is the fact that the intravenous holds no advantage over the intramuscular route in this respect.

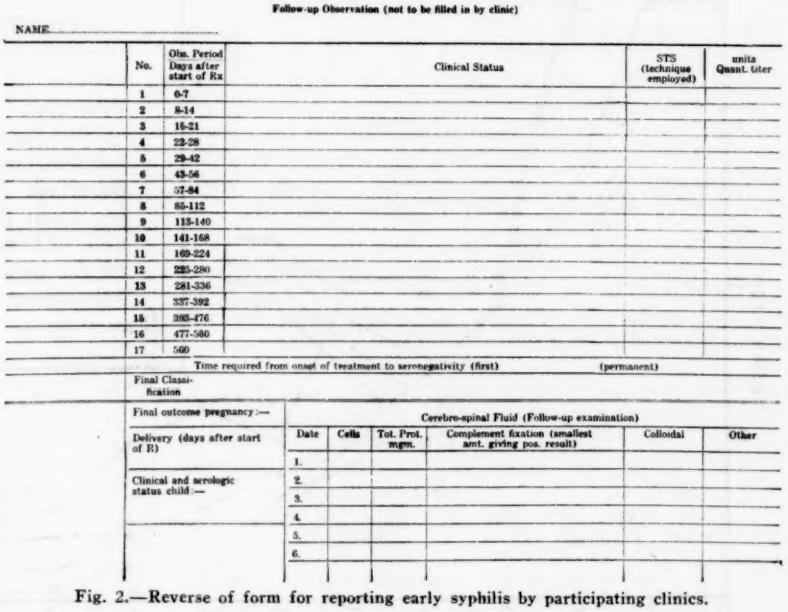
Healing of Lesions.—This is difficult to measure in statistical terms. There has been no observed instance of failure of lesions to heal, regardless of the single or total dose. With a total dosage of 60,000 units in eight days, healing is less prompt than with arsenical therapy; with larger total dosage, 300,000 units and up, it is as rapid as with standard chemotherapy or more so.

Serologic Response.—In figure 3 is shown the median blood serologic response,[7] in terms of quantitative titer, of four groups of patients treated with penicillin alone (excluding those treated with penicillin plus mapharsen). Included are both seropositive primary and secondary syphilis. Regardless of the total dosage, whether 60,000, 300,000, 600,000 or 1,200,000 units, there is apparent a trend toward serologic reversal within a period of about twenty days after the start of treatment. Within the range of 300,000 to 1,200,000 units this trend is approximately uniform, regardless of dosage; with 60,000 units it is a little slower and less pronounced. Parenthetically, this rate of serologic reversal is identical with that observed after arsenical chemotherapy, whether with an arsphenamine at weekly intervals or mapharsen given by various intensive methods.

TABLE 3.—*Average Disappearance Time of Treponema Pallidum from Open Lesions of Early Syphilis After Varying Treatment Schedules (June 1, 1944)*

Size of Individual Dose Given Every Three Hours, Units	Cases	Average Disappearance Time of Treponema Pallidum, Hours
1,000	52	21
5,000	201	20
10,000	237	19
20,000	135	13
40,000	38	14

Further data are shown in tables 4 and 5. In table 4 is summarized the blood serologic response of 48 patients with seronegative primary syphilis observed for nine or more weeks after the start of treatment. These are not broken down by total dosage since, regardless of the range of 60,000 to 1,200,000 units, the response was identical. In 28 patients the serologic test for syphilis, originally negative, remained so throughout the period of observation; in 18 it became temporarily positive, then reverted to negative, and in 2 only there was a subsequent serologic relapse. From the serologic standpoint, therefore, and during the very brief observation period so far available, the results may be said to be satisfactory in 95.8 per cent of the cases.



Follow-up Observation (not to be filled in by clinic)

NAME.....

No.	Obs. Period Days after start of Rx	Clinical Status	STS (technique employed)	units Quant. titer
1	0-7			
2	8-14			
3	15-21			
4	22-28			
5	29-42			
6	43-56			
7	57-84			
8	85-112			
9	113-140			
10	141-168			
11	169-224			
12	225-280			
13	281-336			
14	337-392			
15	393-476			
16	477-560			
17	560			

Time required from onset of treatment to seronegativity (first) (permanent)

Final Classification

Final outcome pregnancy:—

Delivery (days after start of R)

Clinical and serologic status child:—

Cerebro-spinal Fluid (Follow-up examination)

Date	Cells	Tot. Prot. mgm.	Complement fixation (smallest amt. giving pos. result)	Colloidal	Other
1.					
2.					
3.					
4.					
5.					
6.					

Fig. 2.—Reverse of form for reporting early syphilis by participating clinics.

TABLE 4.—*Blood Serologic Response in Seronegative Primary Syphilis, Patients Followed More Than Nine Weeks from Start of Treatment, All Treatment Schedules Combined (June 1, 1944)*

	Serologic Test for Syphilis		
Cases Followed	Negative, Remained Negative	Negative, Became Positive, Later Negative	Serologic Relapse
48	28	18	2

6. Complicated by asymptomatic neurosyphilis, syphilitic meningitis or ocular, osseous or visceral lesions.

7. This has been determined by a statistical device which assigns to the initial quantitative titer, regardless of the actual number of units, the numerical value of 100. All subsequent observations are expressed in terms of per cent of the original titer.

In seropositive early syphilis (combining seropositive primary and secondary syphilis) the results, now broken down by treatment schedule, are shown in table 5 (limited to patients observed for nine or more weeks after the start of treatment). Here there is a direct relationship between "satisfactory" and "unsatisfactory" immediate serologic results and total dosage of penicillin; the larger the dose, the better the result. The only and perhaps a major exception to this is in the group of patients who received 300,000 units of penicillin plus 320 mg. of mapharsen in seven and one-half days. This group shows as good initial results as were shown by patients receiving four times as much penicillin without mapharsen.

So far it is clear that the minimum effective dose of penicillin in early syphilis in man cannot be determined on the bases of disappearance time of surface organisms, healing of lesions or (except very roughly) serologic response since, regardless of total dose, within the range employed the drug is effective in all of these respects. The only available criterion lies, therefore, in the incidence of relapse.

TABLE 5.—*Blood Serologic Response in Seropositive Early Syphilis According to Treatment Schedule, Patients Followed More Than Nine Weeks from Start of Treatment (June 1, 1944)*

Treatment Schedule, Units	Cases Followed	Serologic Test for Syphilis Response: Satisfactory (Reversed, or Titer Falling), %	Serologic Test for Syphilis Response: Unsatisfactory (No Significant Change, or Relapse), %
60,000	38	57.8	42.1
60,000 + mapharsen	26	76.9	23.0
300,000	79	82.1	17.7
300,000 + mapharsen	24	91.6	8.3
600,000	109	88.0	12.0
1,200,000	62	90.3	9.6

Relapse After Penicillin Treatment.—In this material, relapse has been rigidly defined. Any subsequent clinical manifestation of the disease, whether obviously relapse or apparently reinfection, has been classified as clinical relapse. Serologic relapse includes not only those who, originally seronegative or rendered so by treatment, subsequently became seropositive but also those who, still seropositive in low titer, subsequently develop high titer tests.[8] An effort has been made to observe all patients clinically and serologically at weekly intervals for the first two months, every two weeks for another two to three months and at least monthly thereafter.

TABLE 6.—*Incidence of Relapse in Seronegative Primary Syphilis Treated by Varying Schedules in Eight Days, Patients Observed for More Than Thirty-Eight Days (June 1, 1944)*

Treatment Schedule, Total Dose, Units	Cases Followed	Relapse: Clinical	Relapse: Serologic	Relapse: Total Number	Relapse: %
60,000	1	..	..	..	...
200,000	..	..	..	..	...
300,000	14	1	..	1	7.2
600,000	21	1	1	2	9.5
1,200,000	52	..	..	..	...
Intravenous (see text)	4	..	..	..	...
Total	92	2	1	3	3.2

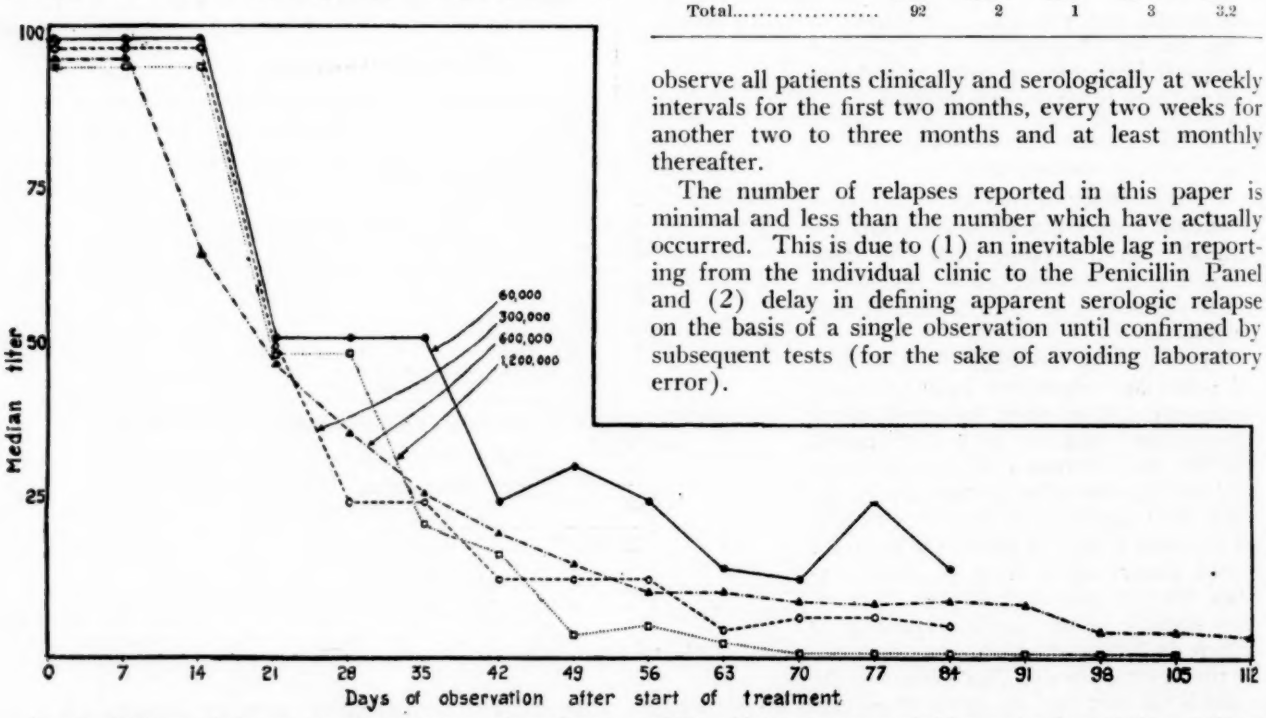


Fig. 3.—Median serologic response of seropositive early syphilis to penicillin with four treatment schedules ranging from 60,000 to 1,200,000 units total dose in eight days; June 1, 1944.

The number of relapses reported in this paper is minimal and less than the number which have actually occurred. This is due to (1) an inevitable lag in reporting from the individual clinic to the Penicillin Panel and (2) delay in defining apparent serologic relapse on the basis of a single observation until confirmed by subsequent tests (for the sake of avoiding laboratory error).

The method of statistical reporting here adopted is recognizedly inaccurate in that the incidence of relapse is related to the total number of patients observed for a period of time greater than that of the earliest observed relapse. In the tables to follow all patients are included who were observed for thirty-eight days or longer after the start of treatment, since this was the shortest interval at which relapse was observed. The brief interval available for study prevents the adoption of the statistical method used by Eagle,[9] which will, however, be utilized in later more definitive analyses. Preliminary rough test of this method of appraisal suggests that the eventual incidence of relapse will probably be from four to five times as great as that reported here. In table 6 is shown the incidence of relapse, clinical and serologic, in 92 patients with sero-

8. Not yet classified as relapse or "unsatisfactory result" are those patients whose serologic tests have shown no improvement. Twelve months after treatment will be allowed to elapse before such patients are classified as seroresistant.

9. Eagle, H.: The Treatment of Early and Latent Syphilis in Nine to Twelve Weeks with Triweekly Injections of Mapharsen: A Preliminary Analysis of the First 4,823 Cases, to be published.

negative primary syphilis. The numbers, broken down by treatment schedule, are too small to be significant, though the total observed relapse rate, 3.2 per cent, is low.

Similar data for seropositive primary syphilis are shown in table 7 and for secondary syphilis in table 8.

TABLE 7.—*Incidence of Relapse in Seropositive Primary Syphilis, Treated by Varying Schedules in Eight Days, Patients Observed for More Than Thirty-Eight Days (June 1, 1944)*

Treatment Schedule, Total Dose, Units	Cases Followed	Relapse			
		Clinical	Serologic	Total Number	%
60,000	8	2	..	2	25.0
200,000	3	..	..	..	....
300,000	30	2	1	3	10.0
600,000	37	..	..	..	....
1,200,000	75	1	1	2	2.6
Intravenous (see text)	5	1	..	1	20.0
Total	153	6	2	8	5.0

TABLE 8.—*Incidence of Relapse in Secondary Syphilis Treated by Varying Schedules in Eight Days, Patients Followed for More Than Thirty-Eight Days (June 1, 1944)*

Treatment Schedule, Total Dose, Units	Cases Followed	Relapse			
		Clinical	Serologic	Total Number	%
60,000	37	9	2	11	29.6
200,000	8	3	..	2	37.5
300,000	94	6	4	10	10.6
600,000	136	4	3	7	5.0
1,200,000	64	..	2	2	3.1
Intravenous (see text)	16	1	1	2	12.5
Total	355	23	12	35	9.8

These relate to patients treated with penicillin alone (excluding the combined penicillin with mapharsen groups). Here there is obvious a direct correlation between total dose and relapse incidence.

The data of tables 6, 7 and 8 are combined in table 9 for all patients with early syphilis; and here is added information concerning the patients treated with penicillin plus 320 mg. of mapharsen (two groups, 60,000 and 300,000 units respectively) and also concerning a small group of patients (25 in number) treated by the intravenous route before the present organized study was begun. In patients treated with penicillin by the intramuscular route the incidence of relapse, even in the brief observation period available, is in direct proportion to total dosage (nearly 30 per cent with 60,000 units, only 2 per cent with 1,200,000 units). In the small group who received large doses intravenously, ranging from 600,000 to 1,200,000 units, and whether by multiple injections or continuous drip, the observed relapses are five to six times as great as in patients treated with comparable doses by the intramuscular route, suggesting that the intravenous route not only holds no advantage over the intramuscular route but is actually less effective.

In table 10 the incidence of relapse is related to the stage of disease at the start of treatment in patients treated with penicillin alone (omitting the groups combined with mapharsen, among which only 1 relapse has so far occurred) and without regard to total dosage. In conformity with Eagle's report [9] as to semi-intensive arsenotherapy, and in contrast to the older Cooperative Clinical Group and other data [10] as to "standard" prolonged arsenical chemotherapy, there seems to be here a direct relationship between the stage of the disease at the time of starting treatment and the incidence of relapse. The proportions in patients treated with penicillin alone are 3.2 per cent for seronegative primary, 5.0 per cent for seropositive primary and nearly 10 per cent for early secondary syphilis.

Table 11 shows the average and extreme intervals between the start of treatment and observed relapse. Here there is no direct correlation as to total dose. Relapses have occurred as early as thirty-eight days and as late as two hundred and ninety-four days after the start of treatment. Considering the short periods of observation so far available for all groups treated, further relapses in all may be confidently anticipated.

The Optimum Time-Dose Relationship for Penicillin in Early Syphilis.—The available data indicate that within the twentyfold dosage range employed in a period of seven and one-half days penicillin has a profound immediate effect in terms of disappearance of surface organisms, healing of lesions and serologic reversal. In seronegative primary syphilis no statements as to minimum effective dose are as yet justifiable. In seropositive primary and early secondary syphilis any dose less than 600,000 units in seven and one-half days is clearly ineffective. A total dose of 600,000 units provides a minimum relapse rate of nearly 5 per cent, of 1,200,000 units a rate of 2 per cent, within the short period for which such patients have so far been followed. The intravenous route appears to be less effective, even in large doses, than the intramuscular.

The possibility that even 1,200,000 units in a four to eight day period will prove to be inefficacious after further observation has led the Penicillin Panel to inaugurate the study of two additional treatment groups

TABLE 9.—*Incidence of Relapse in All Types of Early Syphilis Treated by Varying Schedules, Patients Observed for More Than Thirty-Eight Days (June 1, 1944)*

Treatment Schedule, Total Dose, Units (Route Intramuscular Unless Specified)	Cases Followed	Relapse			
		Clinical	Serologic	Total Number	%
60,000	46	11	2	13	28.2
60,000 + 320 mg. mapharsen	26	..	..	..	....
200,000	11	3	..	3	27.2
300,000	138	9	5	14	10.1
300,000 + 320 mg. mapharsen	68	1	..	1	1.4
600,000	194	5	4	9	4.6
1,200,000	191	1	3	4	2.0
Various intravenous schedules *	25	2	1	3	12.0

* Dosage range 600,000 to 1,200,000 (all but 3 cases 1 million +), single intravenous injections, intravenous drip or both, in 4 to 8 days.

TABLE 10.—*Incidence of Relapse by Stage of Disease, All Treatment Schedules * Combined, Patients Followed More Than Thirty-Eight Days (June 1, 1944)*

Stage of Disease	Cases Followed	Relapse			
		Clinical	Serologic	Total Number	%
Primary seronegative	92	2	1	3	3.2
Primary seropositive	158	6	2	8	5.0
Secondary	355	23	12	35	9.8

* Omitting 94 patients treated with penicillin + mapharsen.

given a total of 2,400,000 units in thirty and sixty intramuscular injections in four and seven and one-half days respectively. These patients are being treated in the United States Army and eight selected United States Public Health Service rapid treatment centers.

The results obtained to date in the two small groups of patients given 60,000 and 300,000 units of penicillin respectively, in each case plus the known subcurative

10. Stokes, J. H., and others: Cooperative Clinical Studies in the Treatment of Syphilis: Early Syphilis, Ven. Dis. Inform. **13**: 165, 207 and 253, 1932.

total dose of 320 mg. of mapharsen in eight days, are worth emphasizing. In 94 such patients followed for thirty-eight days or more only one relapse has occurred. It is perhaps to be expected that certain patients with early syphilis will prove to be resistant to penicillin exactly as a relatively standard proportion of 5 to 15 per cent of patients has proved to be resistant to arsenic heavy metal chemotherapy. But, in view of what is already known concerning the probable modes of action of penicillin and of arsenic and bismuth in syphilis (considerations too lengthy for discussion here) it is possible that those patients resistant to penicillin will not be the same ones resistant to metal chemotherapy and that a combination of the two forms of treatment will eventually prove to be more effective than any method of use of either one alone.

It should also be emphasized that penicillin, as so far employed in early syphilis, is not suitable for mass application. Injections every three hours day and night over whatever period of time demand hospitalization and trained nursing or professional care. However available these may be for the armed forces, facilities are inadequate in civilian practice to meet the enormous demand. The eventual general use of the drug depends on the development of methods which will permit its administration on an ambulatory basis.

TABLE 11.—*Average and Extreme Intervals from Start of Treatment to Relapse According to Treatment Schedule (June 1, 1944)*

Treatment Schedule, Units	Average Interval, Days	Extreme Intervals, Days
60,000	104	64 to 154
60,000 + mapharsen	No relapses observed	
200,000	116	83 to 135
300,000	90	38 to 166
300,000 + mapharsen	..	53*
600,000	98	73 to 113
1,200,000	132	63 to 294
Intravenous	74	56 to 126

* One relapse only.

As with arsenical chemotherapy, it is probable that the optimum time-dose relationship for the treatment of early syphilis in man with penicillin alone and its relative efficacy when administered alone or in combination with other forms of treatment will be guided by data from the experimental laboratory not as yet available but shortly to be expected.

In man, further immediate studies should be directed to (1) determination of the relative effectiveness of 1,200,000 units versus much larger doses in four and eight days respectively, (2) variation of the time interval between individual dosage within the range of three to twenty-four hours, (3) more exact definition of the merits of intravenous versus intramuscular administration and (4) an expansion of the combinations penicillin plus arsenic and penicillin plus bismuth.

Results of Treatment of Special Forms of Early Syphilis.—Thirteen patients with early syphilis in this series had positive spinal fluids before treatment (11 of them group 2, 2 group 3). Of these, the fluid abnormalities disappeared or improved under penicillin treatment alone in 10 within time period ranging from ten to fifty days; 3 were unimproved.

Acute Syphilitic Meningitis.—Ten patients with this complication of early syphilis have been treated, the majority with 1,200,000 units in seven and one-half days. Symptomatic relief has been dramatically prompt in all and, in the majority, spinal fluid abnormalities have disappeared or are rapidly improving.

Treatment Resistant Early Syphilis.—Eight patients, most of them with dark field positive psoriasiform syphilids, persisting in spite of or recurring during metal chemotherapy, have been treated with penicillin, with prompt healing in all and with subsequent serologic behavior similar to that of previously untreated early syphilis.

Infantile Congenital Syphilis.—Not included in the tabular presentations are some 20 infants with early congenital syphilis. The majority of them have been treated with a total dose of penicillin of 20,000 units per kilogram of body weight, corresponding to a total dose of 1,200,000 units in the adult. Their behavior in terms of symptomatic improvement and serologic response is analogous to that of early acquired syphilis in the adult.

The Outcome of Pregnancy.—Though 58 pregnant women with early syphilis have so far been treated, it is too early to speak of any results as to the outcome in the child.

REACTIONS TO PENICILLIN

Herxheimer Reactions.—Of 1,418 patients treated, 846 (59 per cent) have had Herxheimer reactions within the first twenty-four hours. This consists usually of fever alone (685 cases); in the others, exacerbation of secondary skin lesions with or without fever. The fever is usually mild (less than 102 F.), though in 174 cases (12 per cent) the febrile rise has been higher than this level. In no case has the reaction been alarming, nor has it interfered with subsequent treatment.

Other Reactions.—Only 59 patients (41 per cent of the total treated) have had other reactions attributable to penicillin. In 15 there were cutaneous eruptions (8 urticaria, 7 other types of skin rashes, none severe). Seven had mild gastrointestinal reactions, 33 secondary fever, 2 abscessed buttocks and 2 miscellaneous mild disturbances. In no case has penicillin treatment had to be suspended because of reactions from the drug.

SUMMARY

1. An organized study of the effect of penicillin in early syphilis is in progress in an effort to determine the optimum method of use of the drug. The results so far available are preliminary.

2. Penicillin has a profound immediate effect in early syphilis in terms of (*a*) disappearance of surface organisms from open lesions, (*b*) healing of lesions and (*c*) a trend toward serologic reversal.

3. These immediate effects are in general identical within a twentyfold dosage range of 60,000 to 1,200,000 units administered by the intramuscular route every three hours day and night to a total of sixty injections in seven and one-half days.

4. The same immediate effects are apparent within the dosage range of 300,000 to 1,200,000 units given by the intramuscular route every three hours day and night to a total of thirty injections in four days.

5. These immediate effects cannot be utilized to determine the optimum time-dose relationship, which, in man, depends on the incidence of relapse.

6. The incidence of relapse, when penicillin is administered alone, is in direct relationship to the total dosage given by the intramuscular route in a seven and one-half day period, greatest with 60,000 units and least with 1,200,000 units.

7. Relapse appears to be more frequent after intravenous than after intramuscular administration of comparable doses.

8. The lowest incidence of relapse—and the most favorable serologic response—was in small groups of patients treated with 60,000 and 300,000 units respectively of penicillin plus a known subcurative dose of mapharsen.

9. Penicillin has a favorable effect in early asymptomatic neurosyphilis, acute syphilitic meningitis, early syphilis treatment resistant to arsenic and bismuth and infantile congenital syphilis.

10. No opinion can be as yet expressed as to the effect of penicillin in the prevention of prenatal syphilis.

11. The optimum time-dose relationship of penicillin in early syphilis is not yet established. Certainly the minimum dose, especially in secondary syphilis, should not be less than 1,200,000 units; probably it should be more.

12. Herxheimer reactions after the penicillin treatment of early syphilis are frequent but not serious; other reactions, due to penicillin itself, are negligible.

13. Further avenues of study are suggested.

THE ACTION OF PENICILLIN IN LATE SYPHILIS

INCLUDING NEUROSYPHILIS, BENIGN LATE SYPHILIS AND LATE CONGENITAL SYPHILIS: PRELIMINARY REPORT

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These cases are drawn from eight clinics at present engaged in a study of the effect of penicillin on late syphilis, under the general auspices of the Committee on Medical Research of the office of Scientific Research and Development. These, with the names of the responsible investigators, are as follows: University of Pennsylvania (John H. Stokes, M.D.), Cornell University (Walsh McDermott, M.D.), Mayo Clinic (Paul A. O'Leary, M.D.), Boston Psychopathic Hospital (Harry P. Solomon, M.D.), University of Michigan (Udo J. Wile, M.D.), Bellevue Hospital (Evan Thomas, M.D.) and Johns Hopkins University (J. E. Moore, M.D.). Associated with each of them are various co-workers and assistants too numerous to mention here, but to whom due credit will subsequently be given.

Penicillin has distinctly beneficial serologic and clinical effects on neurosyphilis, including early and late manifestations, not excepting tabes and paresis, and including asymptomatic neurosyphilis. Its action on gummatous manifestations of skin, mucosae and bones is so striking and complete that it seems unnecessary to collect further cases merely to demonstrate it as such. In ocular syphilis, simple inflammatory processes respond; later and more complicated lesions such as the optic neuritides and interstitial keratitis recover, relapse, present resistance and residues proportional to damage already done. This statement is probably true of visceral syphilis and of special localized processes and eighth nerve involvement.

These categorical statements are based on a material collected from 182 cases, observed for periods ranging from eight to two hundred and fourteen days after the institution of treatment. The preliminary conclusions are sharply limited by qualifications involving not only duration of observation and small numbers in individual breakdown items but by wide variation in time-dosage relationships and little uniformity as to time and type of test and recheck procedure. No precedents existing, each investigator groped his way into his problem. A considerable part of the material collected from nonuniform records was of such short observation and so "mixed" in therapeutic procedure that it furnished little evaluative worth. The distribution by source, duration of observation and diagnosis is given in table 1. Paresis, a crucial tester of therapeutic effect, heads the list (56 cases) and neurosyphilis totals 122 cases. Observation of sixty days or more was maintained in 44 Pennsylvania, 20 Johns Hopkins, 11 Mayo, 1 Bellevue, 5 New York Hospital and 1 Michigan case, a total of 82 cases.

Notwithstanding the limitations described, the material furnished the basis for demonstrating by both symptoms and laboratory tests (quantitative serologic, spinal fluid examination) the incontestable reality of the effect of penicillin treatment in syphilis. It permits an exploratory breakdown into grades of treatment effect as such, in relation to previous standard treatment; by at least two grades of intensity of penicillin treatment—low intensity (type A) 600,000 to 1,200,000 units of the sodium salt at 10,000 to 25,000 units intramuscularly every three to four hours and high intensity (type B) 2,400,000 to 4,000,000 units at 25,000 to 50,000 units intramuscularly every two to four hours. It was not possible from this material to estimate the difference in effect of hourly variations or unit dose variations, or of intravenous or intraspinal medication.

EFFECT OF PENICILLIN ON THE REAGIN TITER OF THE BLOOD

Irrespective of the system used and in all types of late (excluding latent) syphilis, penicillin causes improvement (reduction) of reagin titer in from about 50 to 60 per cent of 96 late cases in which such data were available (table 2). An initial Herxheimer-like rise or "provocative" effect is observable in about 20 per cent of late cases. Within the period of observation 10 per cent of late cases became completely negative.

In 5 cases of seroresistant syphilis, 1 became negative (low titer to start with) and 4 improved. Herxheimer effect occurred in 1.

In 32 cases of general paresis, disregarding treatment system employed, 16 were serologically improved, 2 reduced to negative.

EFFECT OF PENICILLIN ON THE SPINAL FLUID IN NEUROSYPHILIS

This furnishes probably the most graphic demonstration of the effect of penicillin, because of its multiple quantitative approach. Seven grades of change were

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The authors are members of the Penicillin Panel of the Subcommittee on Venereal Diseases, National Research Council.

The work described in this paper was done under contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and several universities.

Read in a panel discussion on "Penicillin in the Treatment of Syphilis" before the Section on Dermatology and Syphilology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

considered: worse, no change and five grades of improvement as follows: grade 1, reduction in cell count or total protein; grade 2, reduction in both cell count and total protein; grade 3, reduction of cell count, total protein and intensity of colloidal test; grade 4, reduction in cells and protein and in intensity of both colloidal and complement fixation tests; grade 5, return to normal.

In grouping improvements, grades 1 and 2 together were rated as slight, grades 3, 4 and 5 together as definite improvement. Improvement as a whole, however, included grades 2, 3, 4 and 5.

TABLE 1.—*Penicillin Investigation: Late and Miscellaneous Syphilis; Distribution of Material by Source, Duration of Observation and Diagnosis*

Diagnosis	Duration of Observation: Immediate: Less Than 20 Days	20-59 Days	60-99 Days	100-139 Days	140-214 Days	Total Cases
Paresis and taboparesis	11	22	15	4	4	56
Tabes, including primary optic atrophy	6	8	5	2	1	22
Meningovascular neurosyphilis	6	3	3	3	1	16
Asymptomatic neurosyphilis	2	13	8	1	4	28
Benign late skin and bone	4	8	3	0	6	21
Interstitial keratitis	0	5	3	3	2	13
Iritis	0	2	1	0	1	4
Miscellaneous	4	6	5	6	1	22
Total						182
Clinic sources						
Bellevue	1	3	1	0	0	5
Boston	8	8	0	0	0	16
Johns Hopkins	9	23	10	2	8	52
Mayo	7	3	6	1	4	21
Michigan	6	2	1	0	0	9
New York Hospital	1	10	5	0	0	16
Pennsylvania	1	18	20	16	8	63
Totals	33	67	43	19	20	182

TABLE 2.—*Blood Serologic Response to Penicillin*

Type of Syphilis	Herxheimer or Provocative Effect	Improved But Not to Negative	Reduced to Negative	Improvement Temporary	No Change
Late (96 cases)	20	33	10	13	25

TABLE 3.—*Cerebrospinal Fluid Changes Following Penicillin in 107 Cases in Which Repeated Spinal Fluid Examinations Were Available at Some Time After Treatment*

Diagnosis	Slight Improvement: Grade 1 Cells or Protein Reduced	Grade 2 Cells and Protein Reduced	Definite Improvement: Grade 3 Cells Protein Colloid Reduced	Grade 4 Cells Protein Colloid and Wassermann Reduced	Grade 5 Return to Normal	No Change	Worse
Paresis and taboparesis (42 cases)	6	19	4	4	0	5	4
Tabes and meningovascular (25 cases)	4	2	4	7	0	5	3
Asymptomatic (40 cases)	7	5	6	9	1	6	6
Total (107 cases)	17	26	14	20	1	16	13

In a total of 107 cases which had had one or more spinal fluid examinations after completion of penicillin therapy, it appears that 78 cases showed some degree of improvement in spinal fluid findings, 43 slight and 35 definite. The commonest change is a reduction in cells and total protein, but grade 4 improvement is remarkably common, including all four items of the fluid examination. This response is, as would be expected, evident in a higher proportion (1/4) in asymptomatic neurosyphilis than in paresis (1/9). Some of the cases rated as "worse" are, we believe, to be regarded as Herxheimer or flare effects and would probably improve on longer observation. It is interesting that 4 asymptomatic cases accompanied by gummatous benign syphilis were among the 6 asymptomatic cases in which the condition became "worse."

In order to carry the specific touch of conviction to the doubter as to the effect of penicillin on the blood and spinal fluid, we reproduce here serial spinal fluid and blood observations of 6 patients, 3 with late congenital syphilis and 3 with acquired neurosyphilis. It is notable that these effects were secured with low intensity (type A) treatment in all but 1 case.

TABLE 4.—*Penicillin Treatment Series 1 in Case 3; Total Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid: Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	16 units	29	0123	3 plus	4432210000
13	.....	12	0012	2 plus	2211000000
76	2	10	0112	1 plus	3211000000

TABLE 5.—*Penicillin Treatment Series 2 in Case 3; Total Additional Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid: Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
104	16 units	11	0112	20 mg.	2211100000
161	Less than 1	5	0012	20 mg.	2211000000

TABLE 6.—*Penicillin Treatment Series 1 in Case 5; Total Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid: Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	128 units	22	1244	4 plus	1333320000
19	16	8	1244	3 plus	4431100000
55	32	4	0012	Plus-minus	2221000000
86	64	3	0123	30	2221100000
111	64	1	0124	50	2211000000

CASE HISTORIES

CASE 3 (Pennsylvania).—A man aged 38, with acquired syphilis. Primary optic atrophy in tabes, with euphoria, possible taboparesis. Fields (fig. 2) showed sector defect suggesting arachnoiditic or retrobulbar neuritic episode. Original spinal fluid, cells 122, Kolmer Wassermann reaction 4444, Pandy 4 plus, mastic 4442110000, improved to cells 29, Kolmer Wassermann reaction 0123, Pandy 3 plus, mastic 4432210000 by two Swift-Ellis treatments. After the first series of treatments with penicillin (table 4) the patient began to lose ground visually, with slight confusion and increased euphoria. The second series of treatments (table 5) resulted in definite improvement in fields, acuity and mental state.

CASE 5 (Pennsylvania).—A man aged 24 with congenital syphilis with typical stigmas, asymptomatic neurosyphilis, previously treated with forty arsenical and forty bismuth injections, was given the treatment outlined in table 6. He was retreated twenty-eight days later with the results shown in table 7.

CASE 11 (Pennsylvania).—A man aged 18 with congenital syphilis discovered at age 6 and treated with thirty neoarsphenamine injections a year for eleven years showed typical stigmas, neurologic signs, including Argyll Robertson pupils, anisocoria, partial ptosis of the left eyelid, weakness of the left seventh nerve and sluggish reflexes. He was given the treatment outlined in table 8. The ptosis disappeared under penicillin.

CASE 8 (Pennsylvania).—A woman aged 41 with acquired asymptomatic neurosyphilis discovered in blood donation, without symptoms or previous treatment, was given penicillin with the results shown in table 9.

CASE 29 (Pennsylvania).—A woman aged 29 with acquired neurosyphilis experienced sudden diminution of vision, advanced primary optic atrophy. Previous treatment, 1935-1939, consisted of eighteen arsphenamine and thirty-six bismuth injections. Treatment with penicillin (table 10) resulted in no improvement in fields or acuity: right eye 20/400, left eye 20/300.

CASE 50 (Pennsylvania).—A man aged 25 with congenital syphilis, showing typical stigmas and asymptomatic neurosyphilis, had been treated with sixty-two injections of neo-

TABLE 7.—*Penicillin Retreatment Series 2 in Case 5; Total Additional Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
139	64 units	2	0011	40	2211000000
164	64	4	0011	20	1110000000

TABLE 8.—*Penicillin Treatment Series 1 in Case 11; Total Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	16 units	32	1244	4 plus	3332210000
13	4	16	0122	1 plus	2111000000
32	4	8	0011	Plus-minus	1111000000
140	Less than 1	1	0000	30 mg.	1110000000

arsphenamine and 102 injections of bismuth. Results of treatment with penicillin are shown in tables 11 and 12.

CASE 64 (Pennsylvania).—A man aged 37 with acquired syphilis, early paresis (?), showed sluggish pupils and lower cord reflexes and loss of memory. Previous treatment consisted of twenty-two mapharsen injections and nineteen bismuth injections.

SYMPTOMATIC RESULTS IN NEUROSYPHILIS

Since there is a well recognized disparity between symptomatic and serologic response in neurosyphilis, and the symptomatic often outweighs the serologic aspect in importance for the patient, symptomatic responses secured by penicillin in neurosyphilis were next examined. Here it is important to give warning of misinterpretations due to Herxheimer and possibly therapeutic paradoxical effects from overintense initial treatment. It is notable that some patients who did badly at the start improved later and that top notch symptomatic gains followed a low intensity system in some cases.

Penicillin also has a favorable effect in general paresis. Three groups were made up from the material (conceding the inadequacy from the psychiatric standpoint due to record deficiencies): simple demented paresis (grades 1, 2 3); deteriorated paresis (grades 1, 2, 3); progressive paresis (galloping and so on) and symptomatic exacerbation suggesting Herxheimer effect. Improvement was graded 25, 50 and 75 and 100 per cent, the last representing practically complete restoration to normality.

Of 56 cases of paresis and taboparesis, 10 presented no adequate classification data. Of the 46 remaining cases 30 were classified as simple demented, of which

TABLE 9.—*Penicillin Treatment Series 1 in Case 8; Total Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	64 units	103	4444	4 plus	2444411000
17	8	29	1244	2 plus	2221100000
46	32	11	0012	1 plus	2211000000
74	32	6	0112	30	1111000000
102	32	6	0112	40	2211000000
129	8	4	0011	30	1111000000
159	32	8	0122	30	2211100000
178	16	6	0012	30	2221100000

TABLE 10.—*Penicillin Treatment Series 1 in Case 29; Total Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	64 units	148	4444	30 mg.	3331100000
9	64	16	1244	30 mg.	2221100000
30	32	15	0012	30 mg.	2221000000
65	64	4	0122	20 mg.	1111000000
119	32	0	0011	20 mg.	1111000000

TABLE 11.—*Penicillin Treatment Series 1 in Case 50; Total Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	16 units	96	4444	40 mg.	2455555421
8	Negative	21	4444	20 mg.	4443210000
36	32	12	0124	30 mg.	2221000000

TABLE 12.—*Penicillin Retreatment Series 2 in Case 50; Additional Dose 1,200,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
53	Negative	9	0112	30 mg.	2221100000
84	16 units	3	0000	20 mg.	1111000000

TABLE 13.—*Penicillin Treatment Series 1 in Case 64; Total Dose 2,850,000 Units*

After Penicillin, Days	Quantitative Kline (Blood)	Cerebrospinal Fluid			
		Cells	C. S. F. Wassermann (Kolmer)	Protein	Mastic
0	Less than 1 unit	72	4444	40 mg.	3555521000
22	00	5	0011	20 mg.	1111000000
56	00	5	0012	20 mg.	1111000000

only 6 (20 per cent) failed to improve and 1 grew worse. Thirteen, or nearly half, improved 50 per cent or more, including 8 which improved 75 per cent and 1 restored symptomatically to normal. Ten cases improved only 25 per cent. As might be expected,

deteriorated cases (10) made less response, 1 improving 50 per cent, 2 75 per cent and 7 showing no change. The 1 patient with progressive or galloping paresis in Solomon's service died and 1 of Moore's simple demented patients died thirteen weeks after penicillin.

We know of no record of spontaneous remission under the good effects of hospitalization which can

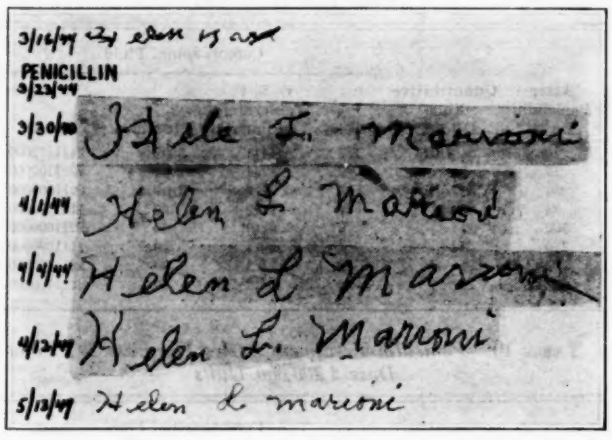

Fig. 1.—Improvement in handwriting of a simple demented paretic patient approximately six weeks after penicillin treatment. The signature before treatment is given above the word "penicillin" (courtesy of George D. Gammon, M.D.).

approach this. The transformations in orientation, speech, handwriting and encephalographic findings will be more fully presented from the University of Pennsylvania material in objective form by George D. Gammon, M.D., in a forthcoming paper. From the collected records, however, two brief summaries are given:

A white woman aged 34 with symptomatic paresis, grade 4 cerebrospinal fluid, could not write or do housework. She had auditory hallucinations, personality changes, disorientation, tremor of the tongue, hands and mouth, and slurred speech. On the second day of penicillin therapy she had a Herxheimer reaction with right-sided convulsions becoming generalized. After twenty-four hours penicillin was reinstituted at half dose to a total of 1,200,000 units without untoward effect. By the sixteenth day the patient was completely oriented, with memory, speech, tremor and electroencephalogram improved. In four months the patient was tremor free, speech and writing were normal (fig. 1), she was well oriented and hallucination free and was satisfactorily performing housework including marketing with points and driving a car. Clinical improvement was not accompanied by improvement in the spinal fluid.

A white man aged 42 with symptomatic paresis developed mispronouncing of words, garbled speech, uncertain gait, tremor of hands and difficulty in writing in August 1943, when a shell exploded near him. Forty-eight arm and hip injections were given. He became boastful, speech rambled and tremors were more pronounced; handwriting was worse and calculation poor. His condition was unimproved during hospitalization after 50,000 Oxford units per dose of penicillin to a total of 4,000,000 units. Clinical improvement occurred three weeks after penicillin with loss of tremors, improved handwriting and speech. He passed an examination as a pipe fitter. Improvement in the cerebrospinal fluid did not accompany clinical improvement. The neurologist considered him mentally improved but not to the original level.

Combining all types of clinically diagnosed paresis and taboparesis, exclusive of 10 patients treated with intraspinal or intravenous penicillin or malaria and thus totaling 46 cases, 15 failed to improve, 12 improved 25 per cent, 6 improved 50 per cent, 10 improved 75 per cent, 1 recovered and 2 died. Of 22 patients with tabes dorsalis, 14 presented data sufficient for interpretation, including 7 with primary optic atrophy and 3 with lightning pains of unusual severity plus 4 taboparetic patients with lightning pains who were grouped together with respect to this symptom. Of the 14 tabetic patients 3 improved to the extent of 50 per cent or more, and 2 of them with lightning pains were relieved completely. Eleven tabetic patients showed no change. Of the patients with primary optic atrophy none were made worse, and 1 whose visual fields are shown (fig. 2) improved slightly but definitely in both fields and visual acuity, with concomitant improvement in the spinal fluid. There is some question as to whether the sector defect in the left field is not a residue of a retrobulbar neuritic process. Of the total of 7 patients with lightning pains, 2 were completely relieved, 1 improved 50 per cent, 2 improved 25 per cent, 1 was unchanged and 1 became worse.

Of 16 patients with various forms of meningovascular neurosyphilis, 6 presented no data on clinical improvement. Of the remaining 10, clinical improvements of 75 per cent were observed in 2, 50 per cent in 2 and 25 per cent in 2, with 3 showing no change and 1 becoming worse.

It is of course difficult to evaluate symptomatology into which elements of the subjective and the influence of suggestion, rest, practice (as in eye and station and gait tests) enter. The intervention of trifling or routine medication (as in the eye, for example) with improvement found to have begun before penicillin, and hence

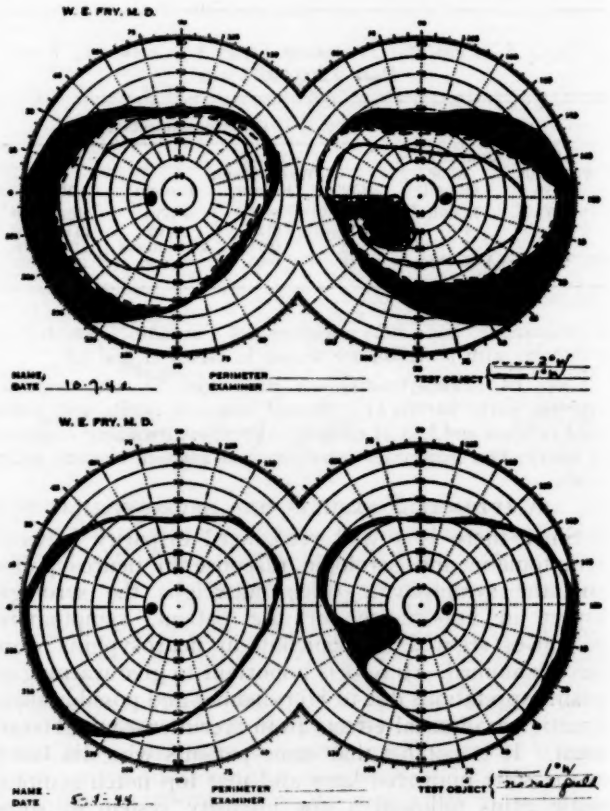

Fig. 2.—Visual fields in case 3, Pennsylvania Penicillin Series, showing improvement with decrease in sector defect.

perhaps merely spontaneous or progressive, must be interpreted by long periods of observation. Symptomatology which is highly complex and of uncertain origin, such as lightning pains, in which the influence of the penicillin on other infective backgrounds may play a part, must be interpreted at this stage with reserve. There seems, however, to be a favorable trend in the

evidence pointing to genuine and indeed rapid good effect on the disease process, supported by such objective detail as handwriting change, encephalograms, disappearance of ptosis and of violent headache associated with meningitis. Coupled with the objective changes in the spinal fluid, such evidence would seem to deserve great weight. It is, however, unreasonable to expect penicillin to restore degenerations and replace neurons.

EFFECT OF TREATMENT SYSTEM

In this material the lack of system in dosage and time intervals reduced the number of cases per recognizable system below statistically usable levels, especially when viewed in relation to duration of observation. Some cases were jumbles of methods and had to be discarded. There were no blood level determinations, and in 3 Mayo Clinic cases spinal fluid penicillin determinations were repeatedly negative. Accordingly, only a study of type A versus type B treatment was attempted, type A representing 1,200,000 units or less, usually at 25,000 units every three to four hours, and type B 2,400,000 units to 4,000,000 units or more at 25,000 to 50,000 every two to four hours. Offhand there was no striking difference recognizable between the effect of shorter time intervals or larger doses except the induction of Herxheimer reactions, which could be avoided by reduction in the dosage of the first twenty-four to forty-eight hours. The analysis of the case material on which treatment information was sufficiently complete for classification, comprising 105 cases, is given in tables 14 and 15.

It must be clearly recognized that such figures as these do not provide for trustworthy therapeutic interpretations. It is particularly in point that the observation periods on the type B (larger dose) treated cases are shorter than those of type A and that a longer observation period may demonstrate a greater efficiency of larger dosage. On the other hand, it is also suggested that in late neurosyphilis good effects may be secured by less than the maximum dosage so far employed. If patients treated with 1,200,000 units in asymptomatic neurosyphilis can achieve almost normal spinal fluids and completely achieve them on retreatment with a similar dosage, a steplike method of successive moderate applications of treatment as distinguished from a single massive session would seem to deserve further study. Pushing the patient over the hump, so to speak, to a partial self cure is a recognized principle in dealing with some aspects of late neurosyphilis.

Serologic response on the blood occurred in 45 per cent of the type A or smaller dose treatment cases, and in 43 per cent of the larger dose or type B cases. Longer observation periods for the type B cases would probably demonstrate a superior effect.

PENICILLIN RESPONSE IN RELATION TO INFLAMMATORY ACTIVITY

Using the cell count and the spinal fluid as a guide and rating 0 to 20 as low, 21 to 60 as medium and 61 and above as high cell counts, an attempt was made to see whether improvement was greater in cases showing a high cell count as an index of definite inflammatory activity in comparison to those showing low cell counts. With cell counts rated as high, improvement occurred in 11 of 31 cases; with those rated as medium, in 13 of 28 cases; in those rated as low, in 7 of 45 cases. It appears that the proportion of improvement is highest in patients with medium and high cell counts in the order named and lowest in patients with low cell counts. If all cell counts above 20 are rated as high, improvement occurs in 24 of 59 cases in the higher cell count brackets (40.6 per cent) and in 7 of 45 in the low cell count bracket (15.5 per cent). Considering the small numbers of cases and the arbitrary division lines, the figures cannot be more than suggestive that, as has been previously indicated, a low cell count has a less favorable prognosis under penicillin treatment than a high cell count.

TABLE 14.—*Effect on Spinal Fluid of Type A (Small Dose) Versus Type B (Larger Dose) Treatment*

	Grade of Response													
	Grade 1		Grade 2		Grade 3		Grade 4		Grade 5		No Change		Worse	
Type of Neurosyphilis	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Paresis and taboparesis	1	5	2	15	1	2	3	1	0	0	1	3	1	2
Tabes	1	3	0	1	0	1	2	2	0	0	0	5	1	0
Meningovascular	0	2	1	1	1	3	3	0	0	0	0	0	0	1
Asymptomatic	1	6	2	3	1	5	4	5	1	0	3	3	6	0
Grade totals	3	16	5	20	3	11	12	8	1	0	4	11	8*	3
Total type A	36		36		36		36		36		36		36	
Total type B		69		69		69		69		69		69		69

* Four of these patients had benign gummas healing under penicillin at a wholly inadequate dosage for neurosyphilis—less than 600,000 units.

Grade 1 and 2 (slight) improvements occurred in 22 per cent of type A and 52 per cent of type B cases.

Grades 3, 4 and 5 (definite) improvement occurred in 16 of 36 cases (44 per cent) on type A treatment and 19 of 69 cases (27.4 per cent) on type B treatment.

Grades 2, 3, 4 and 5 improvement occurred in 60 per cent of the type A and 56 per cent of the type B cases. The periods of observation, however, were longer in the smaller dose treatment cases—e. g., paresis, over sixty days in type A; less than sixty days in all but 5 in type B cases.

TABLE 15.—*Degree of Cerebrospinal Fluid Improvement*

Type of Treatment	Number of Cases	Slight, Grade 1, 2	Moderate to Definite, Grades 3, 4, 5	No Change or Worse
Type A	36	8 (22.2%)	16 (44.4%)	12 (33.3%)
Type B	68	35 (51.4%)	19 (27.9%)	14 (20.5%)

INFLUENCE OF PREVIOUS (ARSENIC, HEAVY METAL) TREATMENT ON PENICILLIN RESPONSE

An analysis of 100 cases of neurosyphilis with data on this matter yielded the results shown in table 16. The results in this case included grade 1 as well as grades 2, 3, 4 and 5. The type of previous treatment approximated the captions given, the first numeral representing arsenical, the second heavy metal injections.

Almost equally good results in the spinal fluid were achieved by penicillin after no previous treatment and intensive (40-80) routine treatment. There is at least no intimation that previous fever therapy prepared the

patients for striking penicillin results. The many qualifications on such an analysis with regard to selection, time of observation and so on must be recalled, but there is at least no strong evidence that in the aggregate previous standard treatment adds anything to the penicillin result.

PENICILLIN IN OTHER ASPECTS OF LATE SYPHILIS

Gummatous lesions of skin and bones (21 cases) respond so invariably and completely, with 13 results rated 100 per cent, 2 at 75 per cent, 4 questionable and only 2 failing of improvement (thirty-six and sixty-eight days), that little further clinical interest attaches to the group beyond speculation as to the part played by penicillin in clearing the secondary, usually hemolytic pyogenic infective invasion as distinguished from the syphilis as such. The control of destructive lesions of the palate and septum seems satisfactory. The failures include one suspected gumma of the orbit, diagnosis not established. The dosage required for symptomatic improvement ranges about 300,000 units, the time for healing from twelve to forty-six days. Carcinoma as a complication or a diagnosis must be watched for

TABLE 16.—*Spinal Fluid and Clinical Improvement in Neurosyphilis After Penicillin Treatment in Relation to Previous Treatment*

Type of Previous Treatment	Clinical Improvement Grade 1 and Over Occurred in:	Spinal Fluid Grades 1, 2, 3, 4, 5 Occurred in:
No treatment.....	16 of 32, or 50 per cent	28 of 32, or 87 per cent
Little treatment.....	9 of 23, or 39 per cent	16 of 23, or 69 per cent
20 arsenic, 20 heavy metal.	7 of 16, or 48 per cent	9 of 16, or 56 per cent
40 arsenic, 80 heavy metal.	5 of 16, or 30 per cent	13 of 16, or 81 per cent
Fever therapy.....	1 of 13, or 7 per cent	5 of 13, or 46 per cent

even if improvement occurs. Concomitant neurosyphilis was identified in 12 of the 21 cases. Serologic improvement (titer reduction) in the blood occurred in 14 of 21 cases.

The paradox of gummatous skin and bone lesions healing as the spinal fluid became "worse" (possible Herxheimer effect?) was noted in 3 of 10 cases.

LATE CONGENITAL SYPHILIS

The interest in this group centers on interstitial keratitis. The neurosyphilitic involvements were reviewed with neurosyphilis (see cases 5, 11 and 50). The complexity of interstitial keratitis and the eccentricities of its behavior are apparent under penicillin as under standard treatment. It was difficult to dissuade those in charge of some patients to withhold fever and other treatment if the patient did not immediately and strikingly improve. Patients with pronounced corneal and other ocular damage were included and too much was expected in the way of results. Of 14 cases 6 showed improvement, 3 of grade 4 on a scale of 1, 2, 3, 4, 1 of grade 3 and 2 of grade 2. Six showed no improvement and in 2 the condition was definitely worse. When improvement occurred it was apt to be dramatic. One patient previously given chemotherapy and fever energetically without result was given 1,200,000 units in eight days. He was relieved of photophobia by the third day and returned to work a week after penicillin for the first time in many months. He has remained well, improvement continuing up to the stage of stationary residue. Another improved grade 4 and one hundred and four days after penicillin flared and recovered again without further treatment. A persistently seronegative congenital syphilitic patient with characteristic stigmas made no response and in fact became worse under 1,200,000 units. One of McDermott's patients, a fever failure, received a total of 4,845,000 units in two courses without results. Thomas secured improvement in a case on 4,000,000 units over twenty-five days, 20,000 units every three hours. Moore has excellent serial color photographs of a favorable case. One of his cases likewise improved on 3,970,000 units in twenty-one days, observed for one hundred and fifty-nine days.

OTHER EYE LESIONS

Two cases of optic neuritis on 2,000,000 and 3,000,000 units both showed improvement; O'Leary's case improved 100 per cent on retreatment. Two cases of iritis improved 100 per cent, but 1 relapsed and required an iridectomy for beginning glaucoma, after failing to respond to retreatment.

EIGHTH NERVE DEAFNESS

Eighth nerve deafness, beginning in a woman of 31 with undoubted stigmas of congenital infection, improved somewhat though not definitely on 1,200,000 units. There was a suggestion of Herxheimer-like drop in hearing at the outset followed by improvement, but the interpretations are complex. Two other cases, already far advanced, failed to improve.

MISCELLANEOUS CASES

A scattered group of cases, on which information is incomplete, includes bone-liver combinations, hepatosplenic complexes, seroresistance (Wassermann fastness) already discussed, Charcot hip and gangrenous balanitis in a syphilitic patient. The Charcot hip did not improve, and a suspected Charcot ankle is developing since penicillin. The gangrenous balanitis healed with the loss of less than a third of the corpus spongiosum on 300,000 units at about the rate to be expected of a late syphilid. The patient became seronegative. The livers of 2 patients undoubtedly enlarged (late cases) after treatment and the blood bilirubin increased in 1, then subsided.

REACTIONS TO PENICILLIN

Penicillin is not a reactionless drug. The disposition to pour it about like water in syphilis may lead to serious trouble, especially from therapeutic shock and possibly also from therapeutic paradoxical effects. The former is important under the usual rule that an active syphilitic process in a vital structure may be gravely and even fatally damaged by the impact of a large dose or series of doses at the start of treatment. Most Herxheimer effects, however, seem controllable by reduction in dosage for the first twenty-four to forty-eight hours of an eight day series without loss of ultimate effect. There is some question whether there are not delayed Herxheimer effects such as are suggested by spinal fluid and blood serologic curves and the initially unfavorable but ultimately favorable course of some lesions (eye, nervous system, for example).

Of 182 cases 43 (24 per cent) had reported reactions interpretable as Herxheimer or therapeutic shock effects. Of these 23 were fever, highest 105.5 F. The blood reagin titer increased definitely and then subsided in 7 cases. In 4 Pennsylvania cases symptoms interpreted as Herxheimer effects in the nervous system included transverse myelitic symptoms in 1 case, jacksonian convulsions lasting twelve hours in another, exacerbation of lightning pains, mania and hallucinations.

Other reactions to penicillin included urticaria (2 cases) and 1 each of "allergic reaction," "id" reaction, burning of the skin, profuse sweating and phlebitis (intravenous injection). Two patients had sharp gastrointestinal reactions.

SUMMARY

From a material of 182 cases of late syphilis preponderantly neurosyphilis (122 cases) and including benign gummatous syphilis, ocular and other forms of syphilis and late congenital syphilis, observed from eight to two hundred and fourteen days after the penicillin therapy was begun on a wide range of time-dosage schedules, the following tentative observations are summarized:

1. The lesions of benign gummatous syphilis of skin and bones heal under a dosage of approximately 300,000 units in twelve to forty-six days.

2. Irrespective of the system used, and in all types of syphilis, pencillin causes reduction of syphilitic reagin titer in the blood in from 50 to 60 per cent of late cases. An initial "Herxheimer"-like or provocative rise is observed in about 20 per cent of cases. Only 5 seroresistant cases were treated, 1 made negative, 4 improved.

3. The abnormal spinal fluid in neurosyphilis is improved in 74 per cent to some degree, definitely in 33 per cent. The commonest change is a drop in cell count and total protein (grade 2 improvement on a scale of 5) occurring in 67 per cent of cases. One spinal fluid was rendered normal within the observation period. All four fluid findings improved in 25 per cent of the cases of asymptomatic neurosyphilis, 10 per cent in paresis and taboparesis.

4. Symptoms improved in neurosyphilis as follows: Simple demented paresis: In 30 cases on which data were adequate for classification, 80 per cent improved to some degree; nearly half improved 50 per cent or more, including 8 who improved 75 per cent and 1 restored to normal. Deteriorated paresis: Two of 10 improved 75 per cent, 1 50 per cent, 7 no change. Tabes dorsalis: One fifth of 14 cases improved 50 per cent or more. Of 7 with lightning pains, 2 were completely relieved, 1 improved 50 per cent, 2 improved 25 per cent, 1 unchanged and 1 worse. Of 7 cases of primary (?) optic atrophy, mostly advanced none were made worse, 1 improved. In meningovascular neurosyphilis 40 per cent improved 50 to 75 per cent.

5. Two attempts at statistical evaluation were made: One, of the influences of smaller dose as contrasted with larger dose treatment and the other, of the response under penicillin of spinal fluids with low as contrasted with relatively high cell counts, because of small numbers of cases and unavoidable disparities in observation period, cannot be accepted as beyond challenge. They suggest respectively that in late syphilis, especially neurosyphilis, smaller doses, if not grossly inadequate, have good effects which may perhaps be improved by repetition, as compared with the effects of initial larger dosage, the effect being due perhaps to stimulation or utilization of the patient's resistance and defensive responses. The figures on response in relation to cell count suggest that moderate and high cell count cases tend to react somewhat better than cases giving low cell counts.

6. Previous treatment for syphilis by older methods in neurosyphilis, including fever therapy, does not appear to prepare patients for superior results with penicillin.

7. In late congenital syphilis, interstitial keratitis presents rather equivocal though at times dramatically favorable results, not as yet interpretable in relation to a time-dosage system. Of 14 cases 6 improved, 3 to 100 per cent, 1 to 75 per cent, 2 to 50 per cent. Two were made definitely worse.

8. Optic neuritis included 2 cases, both improved, the second 100 per cent on retreatment. Two cases of iritis improved 100 per cent at the start, but 1 relapsed and did not respond to retreatment (glaucoma).

9. Two cases of eighth nerve deafness gave equivocal results.

10. Of miscellaneous cases, Charcot joint was unaffected (a new one developing); gangrenous balanitis was cured by low dosage.

11. Therapeutic shock (Herxheimer) effects are undoubted, may be serious in late syphilis and should be guarded against by reduced dosage during the first twenty-four to forty-eight hours. Severe cerebral and cord symptoms may develop in neurosyphilis.

Reactions to penicillin as such are few and not serious, urticaria, itching, allergic skin reactions and a sharp gastrointestinal reaction following the course.

12. It is suggested that, because of the great difficulty in developing uniform records for statistical or punch machine evaluation in late syphilis, further investigation of its behavior under penicillin therapy be committed to individual competent investigators who can apply the principles of uniformity of treatment and record evaluation simultaneously with appropriate individualization of the particular case. The durability of the good effects thus far observed, the possibility of complications from induced allergic response and disturbance of the immunity balance of the individual in latent and late syphilis remain to be explored by larger experience and longer periods of observation.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. MAHONEY, ARNOLD AND STERNER AND MESSRS. HARRIS AND ZWALLY, OF DRS. MOORE AND MAHONEY, COMMANDER SCHWARTZ, LIEUTENANT COLONEL STERNBERG AND DR. WOOD, AND OF DR. STOKES, LIEUTENANT COLONEL STERNBERG, COMMANDER SCHWARTZ AND DRS. MAHONEY, MOORE AND WOOD

LIEUTENANT COMMANDER E. E. BARKSDALE, MC-V(S), U.S.N.R.: As of June 1, 1944 we have treated 161 cases of syphilis with penicillin. Twenty-nine were seronegative, dark field positive, primary syphilis, clinically cured and are still seronegative to date. Eighty were seropositive, dark field positive primaries. Of this group 2 relapsed within approximately three weeks after treatment was started. The lesions recurred in the same location and again became dark field positive. One of this group healed, becoming seronegative, and then acquired a new infection with a dark field positive chancre in a different location from the previous one. We have treated 31 cases of secondary syphilis. All the cases were treated on a dosage of 1.2 million units intramuscularly, i. e. 20,000 units every three hours for sixty injections. By determining quantitative blood penicillin levels on these patients treated with intramuscular injections every three hours, we found that it was impossible to maintain a constant penicillin level, and indeed for one third of the time there was no penicillin detected in the blood by the test used. This made us think that the continuous intravenous drip method might be the procedure of choice. To date we have treated 11 cases of syphilis by this method, giving a total of 2,080,000 units of penicillin in nine days. With this we were able to maintain a more or less constant blood penicillin level approximately ten times higher than that which could be obtained by the intramuscular route. We have had no

relapses, no central nervous system involvement and no case has retained a positive serologic reaction as yet beyond the fourteenth week. To date we have treated 7 cases of syphilis with the usual routine of fever therapy but substituting for mapharsen 60,000 units of penicillin intravenously each time they were in the fever cabinet. In addition and over the same period of time we gave each patient 20,000 units of penicillin intramuscularly every three hours until a total of 3½ to 4 million units had been given. It is our impression that this method is superior to the one which we had formerly used. I am of the opinion at the present time that penicillin is the best drug we have ever had for the treatment of syphilis. I think that it is possible that the intravenous method of administration may be superior. We have had 1 case of primary syphilis treated intramuscularly with 1.2 million units, which ended fatally ten days after the completion of treatment, of a subdural hemorrhage which was not related to either the syphilis or the treatment. Pathologic examination of body tissues with special stains failed to reveal any spirochetes. At autopsy therefore this 1 case within ten days after treatment gave no pathologic evidence of syphilis.

Captain William Leifer, M. C., A. U. S.: The experience at Fort Bragg now comprises 116 patients treated for syphilis with penicillin. One hundred received 1,200,000 units and 16 received 2,400,000 units in seven and one-half days (technic sixty consecutive intramuscular injections of 20,000 or 40,000 units at three hour intervals). Reactions were infrequent and inconsequential: there were 3 instances of urticaria, 1 of erythema multiforme, 2 of generalized pruritus and 7 of herpes simplex. Focal and systemic Herxheimer reactions appeared on the first day of treatment in 87 per cent of the patients. Only those who received 1,200,000 units and who have been followed at least three months are being reported. Ten patients began treatment in the seronegative primary phase and 12 in the seropositive primary phase. Four have been observed over six months, of whom 3 are seronegative, while the fourth has a doubtful Kahn reaction. All 4 had negative spinal fluids at six months. The remaining 18 patients have been followed from three to six months, and all but 1 are seronegative. Thus, 20 of the 22 cases of primary syphilis have achieved or maintained seronegativity. Twenty-five patients began treatment in the secondary stage of syphilis. Two have exceeded six months of observation; 1 is seronegative and the other has a doubtful Kahn reaction. Both had negative spinal fluids at six months. The remaining 23 patients have been followed between three and six months; of these, 11 are seronegative, 9 still have some degree of positivity of the blood and 3 are definitive failures. Two failures appeared as neurologic relapses (1 with monoplegia, the other with acute syphilitic meningitis) with strongly positive spinal fluid; the spinal fluid had been negative in both of these immediately before administration of penicillin. The third failure was a cutaneous and serologic relapse. Thus, of 25 cases of secondary syphilis 12 are seronegative, 10 are still seropositive and 3 are outright failures. It would seem best to use higher doses than might now appear necessary in the treatment of syphilis. The future may reveal the need not only for an increase dosage but also for prolongation of the treatment period beyond the present seven and one-half days. Thus far the results have been extremely encouraging, but mass treatment of syphilis with penicillin should be delayed until the optimal treatment schedule is determined.

Commander Frank A. Ellis, Corpus Christi, Texas: I should like to give you some of the highlights of the experience with penicillin starting in New Zealand in Wellington and extending up to Corpus Christi. An enlisted man with acute infectious jaundice, after being in the hospital five days, developed an acute gonococcic urethritis. His icterus index was 45, and we gave him penicillin; it cured his gonorrhea, and his icterus index was brought down to 0.5. Penicillin might cure acute jaundice or acute infectious jaundice, as we designate it in the Navy. Our results in probably 450 cases of acute gonococcic urethritis have been 100 per cent effective, with this exception: We had 2 cases in which acute epididymitis developed three days after administration of 100,000 units of penicillin. On those we immediately repeated the therapy and gave them 200,000 units until the smears, urine culture and prostatic cultures were negative. My impression is that it certainly shortens the course of acute epididymitis. Our results have been most disappointing in penicillin therapy for nonspecific urethritis. With syphilis I have had no experience whatever except this, that I want to caution you about intraurethral chancre being masked in acute gonorrhea. If patients are given 100,000 units, the dosage will be inadequate.

Colonel Udo J. Wile, U. S. P. H. S.: It is too much to expect of penicillin at this time more than has been graphically told by the authors. We should accept these facts with the possibility that in time the organisms may elaborate for themselves a certain degree of resistance to penicillin. When we can speak in terms of thousands instead of terms of hundreds, we may have more relapses and more recurrences and possibly more reactions. It is, however, a great relief to those of us who have for years felt that we were using dangerous drugs in the treatment of syphilis to find something at least that departs from heavy metals that gives a high index of therapeutic effectiveness and apparently a low toxicity.

Dr. Joseph E. Moore, Baltimore: I close on the same restrained note of optimism which has been voiced to you here. I don't think that penicillin is ready for mass application. I do feel that our attitude ought to be one of hopefulness, but with complete understanding that we are still in the process of learning how to use the drug. We don't know yet, and it is going to be some time before we are sure.

SOME HARMFUL EFFECTS OF RECUMBENCY IN THE TREATMENT OF HEART DISEASE

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Rest of the affected part is a fundamental form of treatment in many diseases. When a bone is fractured, splints are applied and the involved parts are immobilized. This not only diminishes pain but speeds repair and healing. When a lung is actively affected with tuberculosis, attempts are made to diminish the movements of the diseased lung. The phrenic nerve may be sectioned, pneumothorax produced or thoracoplasty performed, the purpose of these procedures being to rest the affected organ. In a similar way when the heart is diseased, rest in bed has been urged as a means of diminishing its work. Not so long ago the relative value of rest and exercise was much debated and was summarized by Pratt,[1] who strongly advocated prolonged rest in bed for heart failure. At present all students and physicians have been forcefully impressed with the great importance of rest in bed, although in practice one finds great variations in the degree to which the principle is applied. Under similar circumstances one physician may keep a patient in bed a few days, another a few weeks and a third a few months. What should be our guide and what are the hazards, if any, of strict bed rest?

At the outset, a clear distinction must be drawn between the function and dynamics of the heart and the conditions that obtain in other organs. One important peculiarity of the heart is that it has two sides, right and left, and that serious difficulties may ensue if an imbalance develops between the two. If the right ventricle expels one drop of blood less than the left ventricle, within a few hours there will be increased

From the Medical Clinic of the Peter Bent Brigham Hospital and the Department of Medicine, Harvard Medical School.

Read at the dedication of the National Institute of Cardiology, Mexico City, Mexico, April 20, 1944.

1. Pratt, J. H.: Rest and Exercise in the Treatment of Heart Disease, South. M. J. **13**: 481, 1920.

venous pressure and pronounced engorgement of the liver. Contrariwise, if the right ventricle expels one drop more than the left ventricle there will result pronounced pulmonary edema. In each instance 250 to 500 cc. of blood would be trapped either in the systemic venous system or in the pulmonary circuit. Similarly it follows that, when there is definite pulmonary congestion, those measures that reduce the return flow to the right side of the heart, and therefore the output of the right ventricle, relieve pulmonary congestion and help to restore the balance between the two sides. We are all familiar with the beneficial effects of phlebotomy or the application of tourniquets to the extremities in this regard.

With the foregoing considerations in mind it is well to analyze the effects of putting a cardiac patient to bed. In general, rest obtained in this way decreases the total bodily demands or basal metabolism, slows the heart rate and may lower the blood pressure. All this decreases the work of the heart. The one factor that has been overlooked, for the most part, is that the effect of recumbency is also to encourage venous return. As the lower part of the legs remain elevated and approximate the level of the right side of the heart, tissue edema more readily disappears through the lymphatics, capillaries and venules. The result of this mechanism is to increase rather than to decrease the work of the right side of the heart. When this effect is considerable and the left ventricle is so weak that it cannot keep pace with the increased output of the right ventricle, during the hours or days of recumbency, pulmonary congestion and resultant breathlessness may actually increase. In other words bed rest, for a while, may impose greater rather than less work on the heart.

All physicians are familiar with the clinical events that take place during an acute attack of nocturnal cardiac dyspnea or so-called cardiac asthma. A patient, generally with hypertension, coronary or aortic valvular disease goes to bed feeling fairly well and about 2 o'clock in the morning is awakened with breathlessness, suffocation and possibly cough and wheezing. He generally jumps out of bed, walks around the floor in his agitation, goes to a window for air or sits up in bed with his feet hanging down. In fifteen minutes or a half hour the attack may be over and he falls back to sleep. Some find that they can sleep the remainder of the night only if they sit in a chair. The surprising thing is that, although our patients have long been aware of the harmful effects of the bed and have dreaded the nights, we as physicians would generally insist that they be put on a strict bed regimen. Many of our patients would emphatically state that they felt quite well while they were up and about, some of them even being able to do quite a bit of work during the day but had all their trouble in bed. With equal persuasion we would maintain that they had to go to bed.

It is true, however, that in most cases when we put such patients to bed no harm resulted. In fact, they generally improved. Often the nocturnal dyspnea disappeared and both the patients and the physician became convinced that bed rest was valuable. Nevertheless a closer analysis will reveal, I believe, that some temporary ill effects were produced but that in most instances the various methods of treatment employed were effective enough to counterbalance and mask them. Only when the entire program of treatment is ineffective do we see gross evidence of the deleterious results that are produced by bed rest. I recall, as many physicians will on close reflection, frequent instances in which shortly after ordering an ambulatory cardiac patient to bed pulmonary rales and hydrothorax, previously absent, quickly appeared. Such a patient may have complained of nocturnal dyspnea and shown no peripheral edema or slight pitting of the legs. The lung bases were clear of rales at that time. Ordinarily with complete bed rest the nights are made comfortable by the use of hypodermics of morphine until the effects of digitalis, diuretics, diet, phlebotomy and other measures have improved the situation so that pulmonary congestion clears and breathing becomes normal. But in the type of case mentioned, for one reason or another the progress is down hill because the customary treatment is not effective enough to undo the harm done by the recumbent posture. Such a patient often shows complete disappearance of peripheral edema but now needs a thoracentesis for a right hydrothorax. Even if no pitting is apparent we must realize that patients may have several liters of latent edema without pitting. It also must be borne in mind that fluid in the legs may be unsightly but does comparatively little harm, whereas fluid in the lungs is a dangerous handicap.

Another illustration of the shift of fluid from the lower to the higher portions of the body in decompensated cardiac patients is the disappearance of pitting edema of the ankles while extensive edema of the lower part of the back develops. Physicians often seem pleased that the ankles have returned to normal size in their cardiac patients who are confined to bed and overlook the fact that the same fluid is still within the body, only now is distributed in its upper portions.

One might ask what evidence there is that it is the bed rest that causes these changes. First, it is the experience of our patients (just cited), who often are our best teachers. Then it is the clinical detection of increasing signs of pulmonary congestion in some cases (while the peripheral signs decrease) coming during the first few days after bed rest has been instituted. Finally, certain laboratory data afford convincing proof to support these clinical impressions. It is known [2] that normally there is a decrease in the total lung volume of over 300 cc. and a decrease in the vital capacity of the lungs of about 200 cc. in the recumbent position. These changes may possibly be greater in patients already suffering from congestive failure. Several years ago [3] I made a few casual observations on the vital capacity of the lung and the velocity of blood flow just before putting cardiac patients to bed and one or two days later. The former was found to decrease slightly and the latter to slow before real improvement began. More recently a systematic study was made by Perera and Berliner [4] on the effect of posture on the dynamics of the circulation in normal individuals and in patients with paroxysmal nocturnal dyspnea. They found that the assumption of the horizontal position caused a decrease in serum concentration and slight increase in venous pressure in both groups. The serum protein was also found to rise toward the normal levels in patients about fifteen minutes after the attacks of dyspnea were over. The

2. McMichael, J., and McGibbon, J. P.: Postural Changes in the Lung Volume, Clin. Sc. **4**: 175, 1939.
3. Levine, S. A.: The Management of Patients with Heart Failure, J. A. M. A. **115**: 1715 (Nov. 16) 1940.
4. Perera, G. A., and Berliner, R. W.: The Relation of Postural Hemodilution to Paroxysmal Dyspnea, J. Clin. Investigation **23**: 25, 1943.

only reasonable interpretation that can be made from these observations, and the conclusion drawn by these authors, is that with recumbency hemodilution and increased blood volume occur as a result of the flow of fluid from the tissue spaces into the blood stream. This obviously is deleterious to cardiac patients, and when there is a tendency to dyspnea from left ventricular weakness or from serious mechanical obstruction of mitral stenosis serious pulmonary edema may result.

An increase in blood volume is one of the most constant findings in congestive heart failure, and effective treatment is always concomitant with a decrease of blood volume toward normal. The observations cited show that recumbency produces, at least temporarily, exactly the effect that is undesirable by increasing the total volume of blood and as a result the work of the heart. It is clear therefore that, although the fundamental principle that rest is beneficial for the heart remains undisputed, the recumbent position in some cardiac patients may actually increase the work of the heart. To be sure, this effect is often temporary; for when sufficient improvement has occurred the left ventricle is able to expel its quota of blood or the right ventricle no longer delivers an excess into the pulmonary circuit and a proper balance has been established. From then on rest in bed does accomplish its purpose in diminishing the total work of the heart.

There are other difficulties that may follow prolonged bed rest both in cardiac and in noncardiac patients. In some elderly men urinary retention from an atonic bladder and prostatic obstruction may first develop after confinement to bed. This may necessitate catheterization with the occasional development of infection and its complications. Many others may develop hypostatic pneumonia, which used to be so often fatal to chronic cardiac patients.

What we have learned to be much more important is the frequent occurrence of thrombophlebitis of the legs with subsequent pulmonary embolism. The medical profession has only in the past few years become aware of the extent and seriousness of this problem. Williams and Rainey [5] even suggested that the initial period of complete bed rest should be reduced, because in a large number of their cardiac patients pulmonary infarction and pneumonia were found to be the cause of death.

In Boston, in large measure as a result of the clinical studies of diseases of the veins by John Homans [6] and the pioneer work on acute cor pulmonale by P. D. White and his associates,[7] we are recognizing more and more cases of pulmonary embolism. As we all know, this is a common cause of death following operations in any surgical clinic. It is equally frequent in the medical wards in hospitals, especially in patients confined to bed for any appreciable time. Immobility of the legs, abdominal distention with its inevitable pressure on the iliac veins, and the sluggishness of the circulation in cardiac patients all result in slowing of the blood flow through the legs, which is conducive to venous thrombosis. This is particularly true of very obese and orthopneic individuals, for in a sitting position there is added constriction of the pelvic veins.

When cardiac patients are examined post mortem and pulmonary emboli or pulmonary infarction are found, one is too ready to explain them on the basis of emboli from the right side of the heart or as a result of local thrombosis of the pulmonary vessels. Only a careful search of the veins of the legs or pelvis will reveal the great frequency of thrombosis, which proves to be the actual origin of these pulmonary complications. This entire situation is serious and in many cases the medical profession is to blame. I know I have been directly responsible for needless fatalities from pulmonary embolism in patients who would have done well had I not put them to bed. As a corollary to the foregoing we should be quick to detect any phlebitis of the leg, especially the deep type of thrombophlebitis. This often starts in the calf and is not manifested by gross swelling of the leg but rather by early pain in the calf on dorsiflection of the foot. Certainly, if a patient with such phlebitis has one pulmonary embolism or some obscure sudden respiratory episode, ligation of the vein should be performed immediately. In fact, my fear of a fatal pulmonary embolism has become so great that I advise immediate femoral vein ligation just as soon as a deep phlebitis is recognized.

The following case reports will illustrate some of the preceding points:

Case 1.—A shopkeeper aged 58 had a typical attack of acute coronary thrombosis April 10, 1937. Severe and increasing breathlessness developed during the following three weeks. At this time (May 3, 1937) I first saw him and found him to be irrational and considerably orthopneic, with Cheyne-Stokes breathing. The lungs were full of rales, but there was no pitting edema of the legs. The heart sounds were distant, regular and rapid. He had been in bed under an oxygen tent most of the time. I advised omitting the various medications he was receiving, such as aminophylline, digitalis and caffeine, and had him placed in a chair with his feet hanging down. Within a few hours his condition began to improve. Two days later he showed edema of the legs, but the orthopnea was practically gone and he was rational. He then received digitalis and mercupurin, had a satisfactory diuresis and gradually recovered compensation. He was still ambulatory and in fairly good health three years later. The turning point in this patient's condition occurred directly after getting him out of bed into a chair. The edema lessened in the lungs as it increased in the legs.

Case 2.—G. H., a business executive aged 66, seen in my office Feb. 1, 1934, had been slightly short of breath for a few years but carried on his work fairly well. Since August 1933 he had frequent smothering attacks, waking him up from sleep. He would have to sit up in bed and get into a chair for relief. During the day, while he was up and about, he was comfortable.

Physical examination showed considerable cardiac enlargement, a grade 2 aortic systolic murmur, a definite gallop rhythm and a definite pulsus alternans. The rhythm was regular, with a rare extrasystole. The breath sounds were much decreased, the liver was slightly enlarged and there was moderate pitting edema of the legs.

He was put on complete bed rest in the Peter Bent Brigham Hospital and assured that he would be made comfortable, though he insisted that he feared the bed. The first few nights were in fact quite comfortable, because he was given hypodermic injections of morphine, which he had never received before. He was also started on digitalis therapy by mouth. Two days after admission, edema of the legs had entirely disappeared; but now a right hydrothorax was present, which was not there when I first put him to bed. The breathing became more labored and of the Cheyne-Stokes type. A right thoracentesis was performed, removing 1,200 cc. of clear fluid on the fourth day; and from then on, with the help of mercurial diuretics, his condition improved. As compensation was regained, the basal systolic murmur became more prominent, an aortic systolic thrill was felt, and x-ray examination showed definite calcific aortic stenosis. After several weeks he became ambulatory and free from dyspnea and edema.

5. Williams, R. H., and Rainey, J.: The Causes of Death in Patients with Congestive Heart Failure, Am. Heart J. **15**: 385, 1938.
6. Homans, J.: Thrombosis of the Deep Veins of the Lower Leg Causing Pulmonary Embolism, New England J. Med. **211**: 993, 1934.
7. McGinn, S., and White, P. D.: Acute Cor Pulmonale Resulting from Pulmonary Embolism: Its Clinical Recognition, J. A. M. A. **104**: 1473 (April 27) 1935.

This is a striking instance of a shift of fluid from the periphery to the chest on putting a cardiac patient to bed. The patient did become worse as a result of the position in bed and showed improvement only when active cardiac therapy caught up with and undid the harm done by recumbency. This might have been avoided if he had been treated in a more upright position or in a chair during the first week.

CASE 3.—E. G. B., a housewife aged 58, came to my office Nov. 27, 1936 complaining of weakness, dizzy spells and inability to lie flat because of shortness of breath and choking feelings. These symptoms began only a few months before she was first seen.

The patient was obese, weighed 98 Kg. and was 61 inches (155 cm.) in height. The heart was entirely normal, the lungs showed a few basal rales, the abdomen was prominent but otherwise not remarkable, and there was slight puffiness of the legs. The blood pressure was 180/105. The urine was normal. The vital capacity of the lungs was much decreased (1,400 cc.). The electrocardiograms were normal.

She was sent to the hospital with a diagnosis of obesity and slight hypertensive heart disease. She was put on a 600 calory diet, kept in bed and given digitalis. She lost about 6 Kg., though there was no diuresis. There was no change in her clinical condition and there was never any evidence of phlebitis of the legs. On December 26 she suddenly developed severe dyspnea. This was erroneously regarded as left ventricular failure, and digitalis, which had previously been omitted, was reinstituted. She remained dyspneic thereafter and died suddenly on Jan. 1, 1937.

Postmortem examination showed some cardiac hypertrophy and dilatation but no cardiac thrombi or significant coronary artery disease. There were numerous pulmonary infarcts and large adherent antemortem clots in each pulmonary artery. A large fresh red friable thrombus was present in the right common iliac vein.

This is an instance of acute fatal pulmonary embolism coming during the course of bed care in an obese hypertensive woman. It seems more than reasonable that this would not have occurred if she had remained ambulatory. Both the immobility of the legs during her period in bed and the pressure of the large abdomen on the pelvic veins, which was accentuated by the sitting position in bed, must have been precipitating factors in the production of thrombosis of the veins of the legs, which led to the pulmonary embolism.

CASE 4.—D. W., a hotel manager aged 52, entered the Peter Bent Brigham Hospital Feb. 10, 1944 complaining of frequent attacks of pain in the midchest. Beginning in February 1941 he had had attacks of pressing pain in the midsternum, radiating into both shoulders and arms. These came on effort, especially walking, and would make him stop, whereupon the attack would let up. The attacks were relieved promptly by glyceryl trinitrate. Despite this he got along quite well until the fall of 1943, when attacks became frequent, even at rest, so that finally he used 10 to 15 glyceryl trinitrate pills daily.

The patient was very obese, weighing 100 Kg. There was no enlargement of the heart, the rhythm was regular and there were no murmurs. The lungs were clear and the abdomen was negative except for prominence due to obesity. No pitting edema was present. The urine was normal. The electrocardiograms showed slight rounding and inversion of T_1, flat T_2 and sharply inverted T_4.

He was put to bed in the hospital because of the frequent attacks of classic angina pectoris. Studies of the blood and other laboratory procedures were not remarkable. He was put on a diet of 1,000 calories, and promptly the attacks disappeared, so that he used only a few glyceryl trinitrate pills during his entire hospital stay, losing 10 Kg. in weight.

Because he had a stout abdomen he found it uncomfortable to lie perfectly flat. He also believed that attacks were more likely to come if he was recumbent. The result was that he sat up in bed most of the time. We were quite encouraged at the quick disappearance of the anginal attacks, when on the twelfth hospital day he developed a slight fever of 101 F. and complained of feeling hot and cold and sweaty. Nothing abnormal could be found on physical examination until two days later, when he had definite pain in the gastrocnemius muscle on dorsiflexion of the left foot. He also had some mild pain in the left calf. The diagnosis of definite thrombophlebitis was made and because of the fear of pulmonary embolism a left femoral vein ligation was performed that very morning. From then on the leg did well, though a slight fever persisted for about ten days. He was ambulatory and much improved when he was discharged March 5, 1944.

This is a clear instance in which putting an obese patient to bed appeared to be directly responsible for the development of a deep phlebitis. Although the anginal state improved, the possibility of a fatal pulmonary embolism was averted only by the prompt ligation of the femoral vein. On retrospect one wonders whether it would not have been better to have him walk around. It certainly was unwise to allow this obese patient to sit in bed with the protuberant abdomen pressing on the veins of the groin a good part of the day.

COMMENT

Evidence has been presented to show that putting cardiac patients on a strict bed rest regimen entails certain hazards. When cardiac congestion is present, recumbency shifts fluid from the lower to the upper parts of the body. Edema fluid leaves the tissue spaces, enters the venous system, increases blood volume and increases venous pressure. These effects are probably temporary and transient in most cases and therefore do not appear to have any deleterious effects on the ultimate progress of the case. Not infrequently, however, this results in an aggravation rather than an improvement in pulmonary congestion, as the return flow to the right heart is enhanced, thereby increasing the output of blood from the right ventricle into the pulmonary vessels. When the left ventricle is still unable to meet this increase in work, as may happen in cases of hypertension, aortic valvular disease or coronary artery disease, dyspnea may grow worse. The same ill effects may be observed in some cases of mitral stenosis, in which the mechanical narrowing of the valve does not permit the added flow to reach the left ventricle. The situation is quite different if there is peripheral edema and engorged liver and there is no important threat of pulmonary congestion or dyspnea. In such cases recumbency will aid in diminishing right sided failure. These considerations do not vitiate the fundamental principle that rest is beneficial for heart failure. In fact, they actually substantiate this principle, because under certain circumstances recumbency is shown to increase rather than to decrease the work of the heart.

It has also become alarmingly apparent that many cardiac patients, after prolonged periods in bed, develop thrombosis of the veins of the legs with serious or fatal pulmonary emboli.[8] This is explained partly on the immobility of the legs and partly as a result of pressure of the abdomen on the pelvic veins. The latter mechanism is very likely of considerable importance in obese individuals or in those suffering from orthopnea who have to sit up in bed. The sitting position assumed

8. Since this article was written, William Dock has published a paper emphasizing this same point, suggesting that pressure of the lower legs on the bed may play a role in causing thrombophlebitis in the gastrocnemius muscles (The Use and Abuse of Bed Rest, New York State J. Med. **44**: 724 [April] 1944).

by such patients must produce added pressure on these veins and thereby slows the circulation in the leg veins.

There are obvious therapeutic implications that follow from the foregoing observations. Some severely ill cardiac patients, especially those with nocturnal dyspnea, should not be kept flat in bed until active cardiac treatment has been well advanced in improving the circulation. During these early days they may sit in a chair and should be urged to exercise their legs or take short walks in their room several times daily. The bed in which they sleep should slant downward from head to foot. This can be accomplished by placing 9 inch wooden blocks under the head posts of the bed. In addition, the required number of pillows under the head should be used. Pillows alone do not meet the difficulty, as the purpose is to have the back and hips higher than the feet. Often it is best to have these patients sleep in beds raised in this fashion the rest of their lives. This may tend to prevent nocturnal dyspnea from returning. At times it is even wise to take a critically sick cardiac patient with severe pulmonary edema deliberately out of bed and place him in a chair with his feet hanging down. The purpose is to shift the fluid from the lungs to the legs. It would be better still if beds that embody this simple principle were generally available for cardiac patients at home and in hospitals.

The second precaution concerning bed care that is applicable to all patients, noncardiac as well as cardiac, who are to stay at rest for any considerable time is to have them exercise their legs frequently during the day. This is a practice that has already come into use to some extent. For the same reason, daily massage to the legs is desirable. The purpose is to prevent thrombosis of the veins of the legs and possible subsequent pulmonary emboli. In this regard, very obese individuals who are inclined to sit up in bed, or orthopneic patients who have to sit in the upright or semirecumbent position, need to be watched with particular care. The sitting position tends to produce pressure on the pelvic veins with slowing of the circulation in the veins of the legs, thus encouraging thrombus formation. It is believed that if attention is paid to the bodily position of the patient while instituting rest treatment our therapeutic results will be improved.

CONCLUSIONS

Rest in bed, which has been the backbone of our treatment of heart failure, needs reconsideration in the light of some possible harmful effects.

There is both clinical and laboratory evidence to show that recumbency may be very harmful for certain patients with heart failure. The heart may be made to work more rather than less, and pulmonary congestion may be made worse rather than better at certain stages of heart failure by placing the patient in bed. Making the bed slant downward by placing 9 inch blocks of wood under the head posts is a simple method of minimizing this undesirable effect. At times it is wise to treat patients with heart disease in a chair rather than in bed.

Cardiac as well as noncardiac patients who are confined to bed for any appreciable length of time should be instructed to exercise their legs frequently or to have massage of the legs to prevent venous thrombosis of the legs and pulmonary emboli.

270 Commonwealth Avenue.

THE ARMY AIR FORCES RHEUMATIC FEVER CONTROL PROGRAM

COLONEL W. PAUL HOLBROOK
MEDICAL CORPS, UNITED STATES ARMY

Rheumatic fever and its sequelae are of far greater significance in civilian life than is generally appreciated. Swift [1] indicates in his survey of New York State for 1938 that there were more than five times as many deaths from rheumatic heart disease as from whooping cough, measles, epidemic meningitis and anterior poliomyelitis combined. He also estimated that there were in excess of 460,000 individuals in the United States with rheumatic heart disease. Acute rheumatic fever has been considered as essentially a disease of childhood, but it has become a very serious problem among adults in the armed forces.

Under the supervision of the Air Surgeon, a program for the control of rheumatic fever and streptococcic infections has been established in the Army Air Forces. Credit for the success of the program belongs to the commanding general of the Army Air Forces, whose cooperation made it possible, and to the many medical and laboratory officers of the AAF hospitals, who have carried on these studies. The basic study was inaugurated in the spring of 1943, with forty of the larger AAF hospitals selected to cooperate in the investigation, representing approximately 25,000 beds and 800,000 troops. The posts chosen for the study were in areas of high incidence of rheumatic fever, areas of low incidence and intermediate areas. The geographic distribution of the areas studied is shown in figure 1. These hospitals, in addition to the usual laboratory facilities present at each, are served by ten strategically located and specially equipped laboratories for the grouping and typing of hemolytic streptococci.[2] Six hospitals located in the areas of lowest incidence were selected to receive patients with rheumatic fever for convalescence. The transfer to these hospitals is usually accomplished by air and can be carried out at a very early stage of the disease. For comparison, control groups are retained in the area in which the rheumatic fever was contracted.

At some air bases the incidence rates for the year 1943 were in excess of 25 per thousand troops involved (figs. 2 and 3). During the peak of the rheumatic fever season one large post experienced rates in excess of 100 per thousand annually. Other geographic areas showed a very low incidence. The total number of new cases for 1943 is large, but statistical data cannot be released at this time.

A consideration of the days lost from duty by this group, the long hospitalization, the large percentage of the group who will be permanently incapacitated, the inevitable compensation for disability and the future necessary medical care by veterans' facilities will indicate to some extent the magnitude of this problem.

The exact etiology and pathogenesis of rheumatic fever is still unknown. Whether it is a sequela disease

Read before the joint meeting of the Section on Practice of Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 16, 1944.

1. Swift, H. F.: Features Which Suggest Public Health Consideration of Rheumatic Fever, Bull. New York Acad. Med. **16**: 501-513 (Aug.) 1940.

2. The special laboratory studies were made possible through the assistance of the Rockefeller Institute, the Josiah Macy Jr. Foundation and the Presbyterian Hospital, New York.

to a group A hemolytic streptococcus infection, the result of a congenital susceptibility, the result of climatic and meteorological factors, a combination of these or due to an agent as yet undiscovered remains for further studies to determine. Our experience and that of others indicates that in the majority of instances the development of the acute rheumatic fever syndrome is related to a preceding hemolytic streptococcus infection. At least it is certain that we have not seen an epidemic incidence of rheumatic fever without a preceding high incidence of hemolytic streptococcus infections. It therefore appears logical to attempt prophylaxis of rheumatic fever in those areas of high incidence by reducing or preventing the hemolytic streptococcus infections and the associated respiratory diseases.

This paper will deal only with one phase of the AAF Rheumatic Fever Control Program and will be limited to a report on the use of sulfadiazine prophylaxis. In March 1943 Painton [3] at the Greensboro Army Air Base, while using sulfadiazine for the prophylaxis of meningococcic meningitis, obtained incidental evidence that scarlet fever could be controlled by this method.

Fig. 1.—Army Air Forces hospitals cooperating in the Rheumatic Fever Control Program, with a notation of special facilities. 1. Westover, Mass. 2. Bradley, Conn. 3. Greensboro, N. C. 4. Seymour-Johnson, N. C. 5. Hunter, Ala. 6. Orlando, Fla. (convalescent). 7. Drew, Fla. (laboratory). 8. Miami, Fla. (convalescent). 9. Patterson, Ohio. 10. Nashville, Tenn. 11. Maxwell, Miss. (laboratory). 12. Keesler, Ala. (laboratory and convalescent). 13. Truax, Wis. 14. Chanute, Ill. 15. Jefferson Barracks, Mo. 16. Barksdale, La. 17. Sioux Falls, S. D. 18. Lincoln, Neb. (laboratory). 19. Salina, Kan. 20. Fort Logan, Colo. 21. Lowry, Colo. 22. Buckley, Colo. (laboratory). 23. Peterson, Colo. 24. Roswell, N. M. 25. Amarillo, Texas (laboratory). 26. Sheppard, Texas. 27. Tarrant, Texas. 28. San Antonio, Texas (laboratory). 29. Fort George Wright, Washington. 30. Gowen, Idaho. 31. Kearns, Utah (laboratory). 32. Luke, Ariz. 33. Davis-Monthan (laboratory and convalescent). 34. Mather, Calif. 35. Hamilton, Calif. 36. Hammer, Calif. 37. Santa Ana, Calif. (laboratory and convalescent). 38. March, Calif.

The control of a scarlet fever epidemic among Navy personnel by the use of sulfonamides was similarly demonstrated by Watson and his associates [4] at the same time. Others [5] have reported favorable effects by the use of small doses of sulfonamides in preventing recurrences of rheumatic fever. Our studies of sulfonamide prophylaxis have been directed toward the determination of optimal dosage, the most effective method of mass administration and an evaluation of the potential danger of the method. In our experience sulfadiazine, because of its low toxicity and availability, has been the drug of choice.

3. Painton, J. F.: Personal communication to the author.

4. Watson, R. F.; Schwentker, F. F.; Fetherston, J. E., and Rothbard, S.: Sulfadiazine Prophylaxis in an Epidemic of Scarlet Fever, J. A. M. A. **122**: 730-733 (July 10) 1943.

5. Hansen, A. E.; Platou, R. V., and Dwan, P. F.: The Prolonged Use of a Sulfonamide Compound in the Prevention of Rheumatic Recrudescences in Children: Evaluation Based on a Four Year Study on Sixty-Four Children, Am. J. Dis. Child. **64**: 963-976 (Dec.) 1942. Kuttner, A. G.: The Prevention of Rheumatic Recurrences, New York State J. Med. **43**: 1941-1947 (Oct 15) 1943. Coburn, A. F., and Moore, L. V.: Prophylactic Use of Sulfonamides in Streptococcal Respiratory Infections, with Especial Reference to Rheumatic Fever, J. Clin. Investigation **18**: 147-155 (Jan.) 1939. Thomas, C. B.: The Prophylactic Treatment of Rheumatic Fever by Sulfanilamide, Bull. New York Acad. Med. **18**: 508-526 (Aug.) 1942.

SULFADIAZINE PROPHYLAXIS

A number of carefully controlled studies were conducted, in which different methods of administration

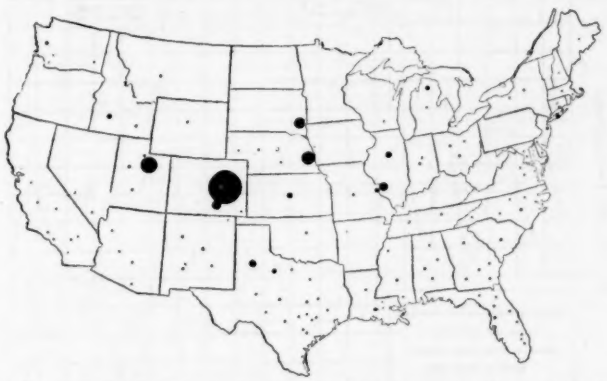

Fig. 2.—Distribution of rheumatic fever in Army Air Forces installations for 1943. The open circles represent posts with rates less than one per thousand annually. The diameter of solid circles is proportional to rates at posts exceeding 1 per thousand annually.

were used and the amount of the drug given was varied. The treated groups and control groups were approximately the same size and represented as nearly as possible identical epidemiologic units. Most of the graphs shown are based on reduction of hospital admissions for respiratory disease and, at these posts, approximately 50 per cent of the admissions for respiratory disease showed clinical and laboratory evidence of significant hemolytic streptococcus infection.

Four grams of sulfadiazine given in a forty-eight hour period produces a definite but very brief reduction in hospital admissions for respiratory disease (figure 4,

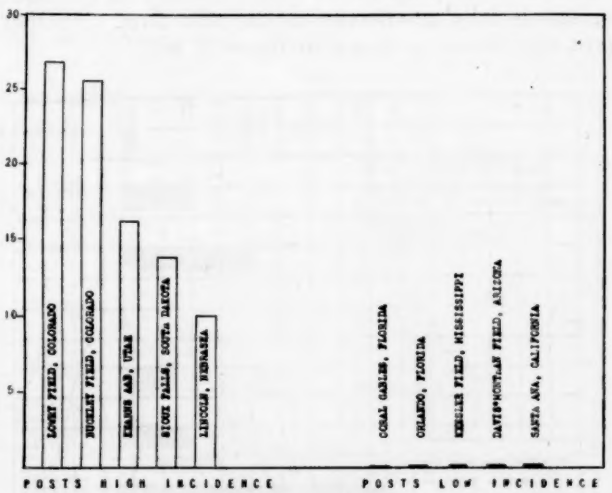

Fig. 3.—A comparison of yearly incidence rates for rheumatic fever in two selected groups of AAF installations.

group B, approximately 5,000 troops). Six grams given over a period of three days promptly reduces the hospital admissions approximately 75 per cent for a period of about twelve days (fig. 4, group A, approximately 5,000 troops). One gram daily effects a continuous reduction in hospital admissions for respiratory disease and is somewhat more effective than the intermittent method if it is not properly timed (fig. 5, 5,000

troops in each group). The efficacy of 1 Gm. daily is clearly shown in relation to the control group in figure 6 (9,000 troops).

Striking reductions are obtained for total dispensary admissions by the same method (fig. 7, 9,000 troops). At two large bases almost identically satisfactory results

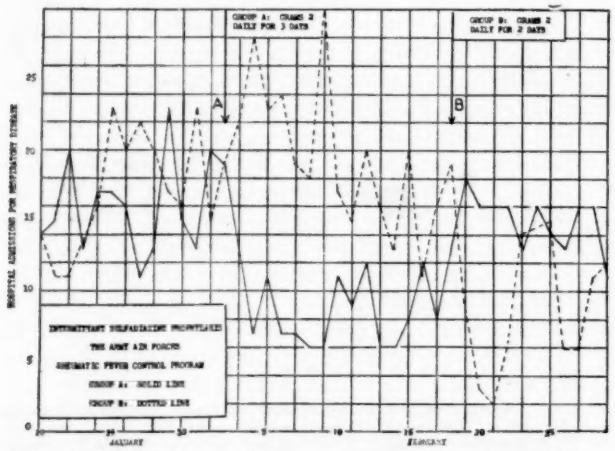

Fig. 4.—Sulfadiazine prophylaxis: A comparison of the effect of varying total dosage in control groups each containing 4,800 troops. Group A, solid line, 2 Gm. daily for three days. Group B, broken line, 2 Gm. daily for two days.

have been obtained in the reduction of the number of admissions to hospitals and dispensaries by the use of 0.5 Gm. daily.

When the effects of sulfadiazine prophylaxis are considered only in relation to streptococcic infections, the prophylactic value is even more dramatic, as might be expected (fig. 8, 4,800 troops in each group). This experience also indicates that intermittent and continuous dosage may be equally effective if properly timed. It further points out that, after a lapse of considerable time, prophylaxis when repeated on the same groups is fully as effective as the first time. Another post experience is shown in figure 9.

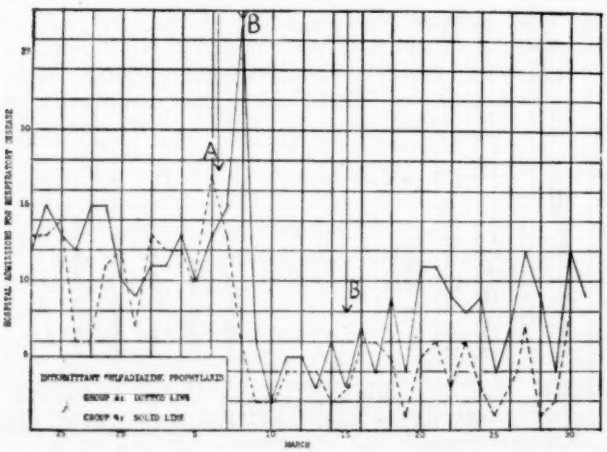

Fig. 5.—Sulfadiazine prophylaxis: A comparison of daily and intermittent dosage in two epidemiologically similar groups of 4,800 troops. Group A, broken line, 1 Gm. daily for twenty-two days; group B, solid line, 2 Gm. daily for two days.

With regard to the reduction in rheumatic fever, total figures are not yet available; but it appears from considerable data at hand that the reduction in rheumatic fever parallels the reduction in respiratory diseases and streptococcic infections.

DRUG REACTIONS

Painton [3] at Greensboro Army Air Base in March 1943 gave each of 18,000 troops 4 Gm. of sulfadiazine in twenty-four hours without serious reactions.

Lee [6] at Santa Ana Army Air Base gave each of 25,000 troops 2 Gm. in one dose and observed thirteen severe reactions. No deaths occurred. Seven had fever and all 13 had skin reactions. There were 15 additional cases of mild skin reactions. The very severe reactions occurred in individuals subsequently found to have a previous history of sulfonamide reactions that were not reported. Our special study of reactions has been limited to approximately 40,000 troops on which full reports are available. There were no deaths. Thirteen individuals lost some days of duty and 33 had mild manifestations not resulting in loss of time from duty. There were no renal complications and no evidence of neutrophilic leukopenia. The major disabilities were skin lesions occurring between the first and sixteenth days of administration of the drug. These disappeared when the drug was discontinued. In the only 2 indi-

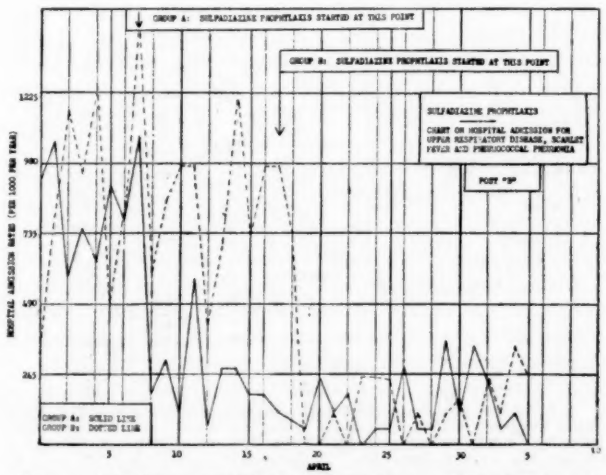

Fig. 6.—Sulfadiazine prophylaxis: The effect of a daily dose of 1 Gm. on hospital admissions for upper respiratory disease, scarlet fever and pneumococcic pneumonia. The two control groups represent 9,000 men. Group A, solid line; group B, broken line.

viduals who developed high febrile reactions there was a history of previous sulfonamide reactions which had not been reported. One patient developed anemia, hemolytic in type, with prompt recovery following transfusions.

Of the 40,000 in this group, only 0.03 per cent lost time from duty and only 0.12 per cent had any type of reaction. Painton's experience with larger doses was similar. The reason for the increased incidence and severity of reactions observed by Lee at Santa Ana is not clear. Larger single doses have been used at a number of AAF installations for prophylactic purposes without a similar result. It is, of course, possible that by chance twice as many reactors were present in his group. However, the possibility of more sunshine at Santa Ana in consideration of the photosensitizing properties of sulfadiazine should be considered. At any rate it is quite obvious that the total hazard is very small and that, if known sulfonamide reactors are eliminated, doses of 0.5 to 1 Gm. daily can be given with almost complete lack of risk.

6. Lee, R. V. A.: Personal communication to the author.

COMMENT

Our army of seven million troops spent in excess of fourteen million days in the hospital last year because of common respiratory diseases. In addition to this time there were the inevitable number of complications and deaths as well as additional millions of man days lost from duty. If our experience with sulfadiazine prophylaxis holds true, it is a conservative estimate that 50 to 75 per cent of this tremendous loss could be avoided.

One question that will immediately present itself concerns the possibility of producing dangerous strains of sulfonamide resistant organisms. The answer cannot be given with complete certainty at this time. However, it is well known that patients who have had prophylaxis in the past respond equally well to sulfadiazine when an acute illness develops. Furthermore, as shown in figure 8, approximately ten thousand troops responded as well to a second period of prophylaxis as to the first. If sulfadiazine prophylaxis is to result in the production of dangerous sulfonamide resistant

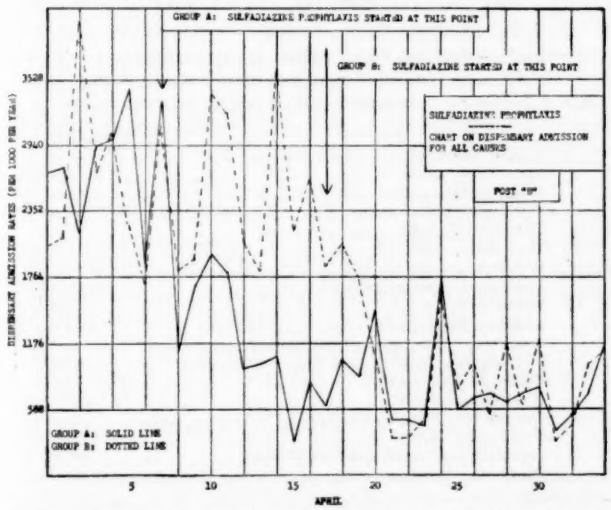
GROUP A: SULFADIAZINE PROPHYLAXIS STARTED AT THIS POINT
GROUP B: SULFADIAZINE STARTED AT THIS POINT
SULFADIAZINE PROPHYLAXIS
CHART ON DISPENSARY ADMISSION FOR ALL CAUSES
POST "B"
GROUP A: SOLID LINE
GROUP B: DOTTED LINE
APRIL

Fig. 7.—Sulfadiazine prophylaxis: The effect of a daily dose of 1 Gm. on dispensary admissions for the same group shown in figure 6. Group A, solid line; group B, broken line.

strains, it would seem reasonable to expect that some evidence of this would already have appeared in our repeated experience on thousands of troops. To the best of our knowledge, such evidence has not yet appeared. Further bacteriologic studies are being directed toward this phase of the investigation.

The possibility of individuals becoming sensitized to the drug on a mass scale has been considered. Repeated periods of prophylaxis on the same groups have failed to demonstrate any developing sensitivity. Following the feeding of sulfonamides, late lesions developing in rats have been reported.[7] Prophylactic doses used clinically are so minute when considering body weight that similar findings in human beings appear extremely unlikely. Further studies on animals, using comparable amounts of the drug based on body weights or blood levels over varying periods of time, should be undertaken. Three months has been the longest continuous period of prophylaxis used by us.

7. Endicott, K. M.; Kornberg, A., and Daft, F. S.: Lesions in Rats Given Sulfathiazole, Sulfadiazine, Sulfanilamide, Sulfamerizine, Sulfapyridine or Acetylsulfadiazine in Purified Diets, Pub. Health Rep. **59:** 49-55 (Jan. 14) 1944.

CONCLUSIONS

1. Acute rheumatic fever shows a striking geographic variation in its distribution, as indicated by the incidence rates per thousand troop population in the various geographic areas.

2. Acute rheumatic fever occurring in high incidence during this study in every instance has been preceded by a high incidence of hemolytic streptococcus infections.

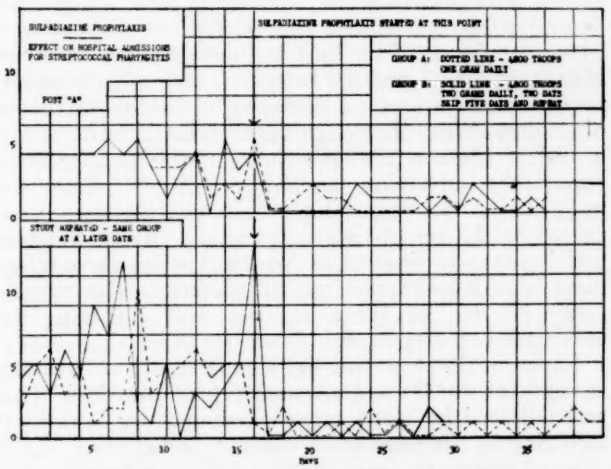
SULFADIAZINE PROPHYLAXIS
EFFECT ON HOSPITAL ADMISSIONS FOR STREPTOCOCCAL PHARYNGITIS
SULFADIAZINE PROPHYLAXIS STARTED AT THIS POINT
POST "A"
STUDY REPEATED - SAME GROUP AT A LATER DATE
DAYS

Fig. 8.—Sulfadiazine prophylaxis: The effect of continuous and intermittent sulfadiazine administration on hospital admissions for streptococcic pharyngitis. The same group of 9,600 men was used in each of the two studies, which were done at an interval of one month.

3. A 50 to 75 per cent reduction in the incidence of respiratory diseases and streptococcic infections has been accomplished by the use of sulfadiazine prophylaxis under carefully controlled conditions and on a significantly large troop population. No serious drug reactions occurred.

4. From the partial data at hand, it appears that the reduction in rheumatic fever parallels that of respiratory and streptococcic diseases.

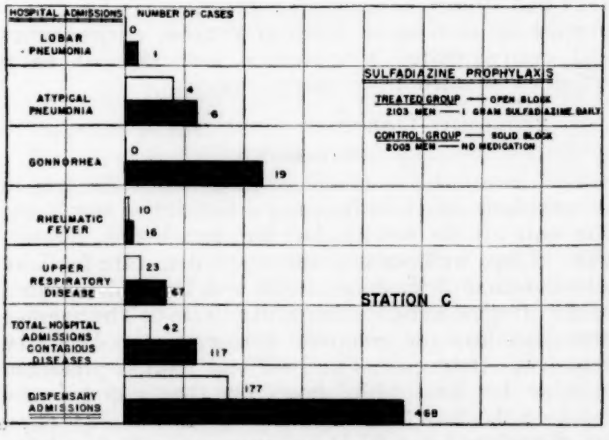

Fig. 9.—Sulfadiazine prophylaxis: Hospital and dispensary admissions for a twenty-one day period from a group of 2,103 men receiving 1 Gm. daily as compared with a control group receiving no medication.

5. The possibility of utilizing these prophylactic methods, thus saving millions of hospital days, avoiding serious complications and adding millions of effective man days to the war effort, should be given consideration.

Office of the Air Surgeon.

THE PREVENTION OF RESPIRATORY TRACT BACTERIAL INFECTIONS

BY SULFADIAZINE PROPHYLAXIS IN THE UNITED STATES NAVY

COMMANDER ALVIN F. COBURN, MC-V(S) U.S.N.R.
WASHINGTON, D. C.

The struggle between bacterial flora and the human host is a continuous one. Survival of the two has been determined by a balanced relationship. In time of war, living conditions of the host are such that this relationship is disturbed, and the balance is now already tipped in favor of respiratory pathogens. In the first year of World War II a significant development in the armed forces was the increasing morbidity rate from respiratory infections, and in the U. S. Navy the majority of the important respiratory diseases were caused by the hemolytic streptococcus. At U. S. naval training centers situated in Northern states these infections have handicapped recruit training. The experiences of one of these stations will illustrate the importance of streptococcic infections in the U. S. Navy.

Early in 1943 a training center with an average strength of 43,000 had an outbreak of measles. This was followed by many types of respiratory infections, including in one year 4,973 cases of scarlet fever, 1,375 cases of rheumatic fever, 1,383 cases of pneumonia, 131 cases of meningitis and at least 50,000 infections of the nasopharynx or tonsils. During the summer months the activity of the meningococcus and the pneumococcus subsided. However, the hemolytic streptococcus maintained its pathogenicity, and late in 1943 this bacterium manifested an increased virulence. It became highly communicable; it produced rather intense scarlet fever; it precipitated severe rheumatic attacks in susceptible subjects; it became invasive. The acquisition of invasiveness by this micro-organism was accompanied by the rapid development of lytic phenomena in the patient, e. g. vomica formation, pericarditis, empyema and other suppurative lesions. Furthermore, strains of this bacterium identified serologically as types 17, 1 and 19 maintained their pathogenicity when transplanted by carriers to other geographic environments and even initiated streptococcic outbreaks at naval activities situated in Southern states.

ECONOMIC LIABILITIES OF STREPTOCOCCIC INFECTIONS

Each man who is taken up on the sick list with a streptococcic infection becomes a liability to the Navy. Not only are his services lost but, in addition, the services of two well persons are required to care for him. The duration of his time on the sick list is determined by the streptococcus syndrome manifested. The average man-days loss for common diseases induced by the hemolytic streptococcus in 1942 and 1943 is presented in table 1. This table shows that the average time spent on the Sick List for scarlet fever was 21.9 days, for rheumatic fever 92.1, for pneumonia 26.4 and for tonsillitis 5.7 days.

Bacterial respiratory tract infections are costly not only in man-days loss but also in dollars expended. For example, the liability incurred for just four of these diseases at a single training station is conservatively estimated as shown in table 2.

A PROGRAM FOR THE CONTROL OF STREPTOCOCCIC INFECTIONS

The Navy's enormous loss to Streptococcus haemolyticus was only one of the compelling reasons for instituting a streptococcus control program. For military and civilian welfare it became essential to prevent the dissemination of the streptococcus among naval personnel, to prevent the induction of rheumatic fever with the development of incapacitating heart disease, to prevent the invasion of the streptococcus into deep tissues with the formation of suppurative lesions and to prevent the spreading of this highly virulent organism from one naval activity to another. To attain these objectives the U. S. Navy instituted a long term streptococcus control program in November 1943.

The first objective in this program was to check the dissemination of respiratory pathogens in the winter of 1944. For this purpose the use of prophylactic doses of sulfadiazine seemed the method of choice. Other investigators had previously indicated the effectiveness of sulfonamide prophylaxis;[1] nevertheless, it seemed wise to control the administration of sulfadiazine with caution. To test the applicability of mass prophylaxis under controlled conditions and to determine a standard prophylactic dose of sulfadiazine, programs were designed for five large Northern training stations with high respiratory disease rates. Groups of trainees were then selected to receive sulfadiazine prophylaxis and comparable groups to serve as untreated controls. At each station these groups were placed under the surveillance of a Navy epidemiology unit consisting of two to five medical officers and four to ten pharmacist

TABLE 1.—*Average Days Spent on the Sick List in 1942-1943 for Diseases Initiated by Respiratory Tract Pathogens*

Diagnosis	Man-Days Loss
Scarlet fever	21.9
Tonsillitis, acute	5.7
Pharyngitis, acute	5.5
Catarrhal fever, acute	4.9
Laryngitis, acute	6.2
Bronchitis, acute	8.5
Tracheitis, acute	6.8
Tracheobronchitis, acute	10.5
Rhinitis, acute	5.2
Angina, Vincent's	8.4
Sinusitis, acute, group (pansinusitis, sinusitis: ethmoidal, frontal, maxillary, sphenoidal)	15.8
Otitis media, acute	10.8
Mastoiditis, acute	60.6
Pneumonia, bronchial	26.4
Pneumonia, lobar	25.8
Cerebrospinal fever (meningococcic)	39.5
Rheumatic fever	92.1

From the Bureau of Medicine and Surgery, Navy Department.
U. S. Navy Epidemiology Units numbers 67 and 89 supplied data used in this report.
Read before the joint meeting of the Section on Practice of Medicine and the Section on Experimental Medicine and Therapeutics at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 16, 1944.
This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

1. Watson, R. F.; Schwentker, F. F.; Fetherston, J. E., and Rothbard, S.: Sulfadiazine Prophylaxis in an Epidemic of Scarlet Fever, J. A. M. A. **122**: 730-733 (July 10) 1943. Thomas, C. B., and France, R.: Preliminary Report of Prophylactic Use of Sulfanilamide in Patients Susceptible to Rheumatic Fever, Bull. Johns Hopkins Hosp. **64**: 67-77 (Jan.) 1939. Thomas, C. B.; France, R., and Reichsman, F.: The Prophylactic Use of Sulfanilamide in Patients Susceptible to Rheumatic Fever, J. A. M. A. **116**: 551-560 (Feb. 15) 1941. Hansen, A. E.; Platou, R. V., and Dwan, P. F.: Prolonged Use of a Sulfonamide Compound in Prevention of Rheumatic Recrudescences in Children: Evaluation Based on Four Year Study of 64 Children, Am. J. Dis. Child. **64**: 963-976 (Dec.) 1942. Kuttner, A. G., and Reyersbach, G.: The Prevention of Streptococcal Upper Respiratory Infections and Rheumatic Recurrences in Rheumatic Children by the Prophylactic Use of Sulfanilamide, J. Clin. Investigation **22**: 77-85 (Jan.) 1943. Chandler, Caroline A., and Taussig, Helen B.: Sulfanilamide as a Prophylactic Agent in Rheumatic Fever, Bull. Johns Hopkins Hosp. **72**: 42-53 (Jan.) 1943.

mates, all of whom had been trained in epidemiology. The duties of each unit included the following:

(*a*) To supervise the distribution of sulfadiazine by line officers.

(*b*) To administer the collection of clinical data on all men reporting to sick bay with respiratory symptoms.

TABLE 2.—*Liability Incurred for Four Diseases at One Training Station*

Disease	No. of Cases	Estimated Days Lost
Scarlet fever	4,973	108,908
Rheumatic fever	1,375	126,637
Pneumonia	1,383	36,511
Tonsillitis or pharyngitis	50,000	285,000
Total days lost to four diseases		557,056
Days consumed by personnel caring for these diseases		1,114,114
Estimated cost in salaries		$5,000,000
Estimated cost in pensions for disabilities		$10,000,000
Total cost for four streptococcus manifestations at one naval training station		$15,000,000
Total man-days loss for four streptococcus manifestations at one naval training station		1,671,171

(*c*) To check the diagnoses of all men receiving sulfonamide compounds who were admitted to the sick list with respiratory infections.

(*d*) To obtain throat cultures on all such individuals and a sample (10 per cent) of individuals contracting respiratory infections in untreated control groups.

(*e*) To isolate the beta hemolytic streptococcus and ship these organisms in pure culture to the National Naval Medical Center, Bethesda, Md., for grouping, typing and testing of drug fastness.

On Dec. 1, 1943 this controlled program was initiated at five training stations. Data on the incidence of respiratory infections in the "treated" and control groups were collected for three months. With the accumulation of these data the effectiveness of mass prophylaxis was manifest. It was then decided to extend the program to three other naval activities experiencing a high incidence of streptococcic infections

TABLE 3.—*Monthly Morbidity for Certain Diseases Activity A*

Rates per Thousand Men During the Winters of 1943 and 1944

Diagnosis	1943			1944		
	January	February	March	January	February	March
Tonsillitis	15.1	8.6	25.8	25.0	13.0	**2.9**
Catarrhal fever	75.1	58.2	76.3	54.2	26.6	**5.6**
Scarlet fever	0.5	2.8	9.3	16.6	4.4	**0.8**
Rheumatic fever	3.5	3.9	3.2	8.6	4.3	**1.3**
Septic sore throat	0.0	0.0	0.1	3.5	1.6	**0.5**
Pneumonia, bronchial	0.0	0.0	0.0	1.6	3.4	**0.4**
Pneumonia, lobar	0.5	0.0	0.6	1.3	1.7	**0.2**
Pneumonia, atypical	2.1	2.7	5.2	0.1	0.3	0.5
Sinusitis	3.7	3.6	5.1	6.7	5.0	**1.8**
Pharyngitis	1.7	0.8	4.5	1.4	6.0	**1.3**
Laryngitis	0.2	0.4	0.4	0.9	0.5	**0.2**
Otitis media, acute	2.3	3.2	6.3	6.0	5.6	**1.8**
Vincent's angina	2.5	2.0	1.8	0.1	0.0	0.5
Bronchitis	0.6	0.4	1.1	0.4	0.0	0.4
Meningitis	0.1	0.6	0.2	1.7	0.2	**0.1**
Mastoiditis, acute	0.0	0.0	0.1	0.4	0.2	**0.1**

and to discontinue the use of untreated controls in the five naval activities at which the sulfadiazine program was already in operation. Continuous mass prophylaxis was accordingly extended to about fifty camps of eight naval activities, and this program was continued throughout the spring months. The effectiveness of the overall program will be appraised in a forthcoming monograph.[1a] The present paper is a preliminary report limited to observations on sulfadiazine prophylaxis instituted under three different conditions at three naval training camps.

1a. Nav. Med. 284.

THE EFFECT OF SULFADIAZINE PROPHYLAXIS INITIATED DURING A STREPTOCOCCIC OUTBREAK AT ACTIVITY A

Naval Activity A, situated in the city of Chicago, had experienced a high rate of infections occasioned by the great expansion of intensive training with a rapid turnover in personnel. Early in the winter its training program was seriously handicapped by a high incidence of streptococcic infections, which were subsequently identified as due to types 17, 3 and 30. During December 1943 more than 25 per cent of the station's complement were admitted to the sick list with respiratory infections, in all 27,966 man-days, or about 10 per cent of the available man power, were lost. The incidence of these infections continued to be high in January, and a large number of men developed rheumatic fever. By February 1944 the hospital admission rates [2] for respiratory diseases and sequelae had reached extraordinary heights: for catarrhal fever 988, for tonsillitis 426, for scarlet fever 171 and for rheumatic fever 70. The urgency of the situation and the expectancy of an increase in these rates during February and March

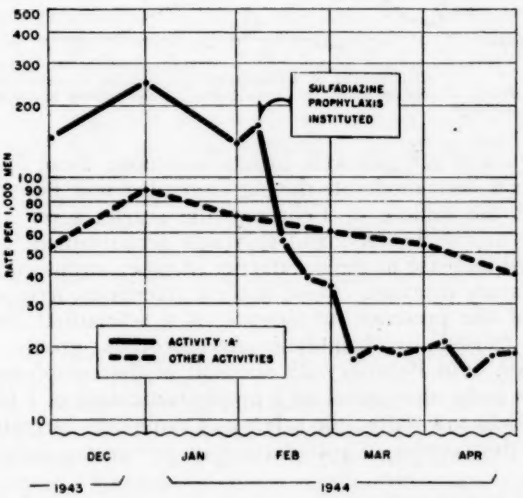

Chart 1.—A comparison of the monthly morbidity rates for respiratory tract infections at Activity A with those of other naval activities in the Chicago area.

were cogent reasons for placing all station personnel on sulfadiazine prophylaxis.

Results of Sulfadiazine Prophylaxis.—The institution of prophylaxis, 1 Gm. of sulfadiazine daily, on February 8 was followed by a rapid fall in the incidence of disease. For example, the scarlet fever rate [2] fell weekly to 70, to 45 and to 0 during the third week. The rheumatic fever rate rose during the first week of prophylaxis to 87 and then fell progressively by weeks to 45, 45, 19 and 6. The fall in incidence of respiratory diseases observed in February became even more pronounced in March and April 1944. That this was not to be expected from the experience of 1943 is shown in table 3. And it is seen in table 4 that this phenomenal change was not observed at other naval activities in Chicago during March and April 1944. A comparison of the monthly morbidity rates for respiratory infections at Activity A receiving sulfadiazine prophylaxis after February 8 and for five other naval activities in Chicago receiving no prophylaxis is shown in chart 1.

In summary, the institution of sulfadiazine prophylaxis 1 Gm. daily to all hands at Activity A on

2. Annual admission rates per thousand strength.

February 8 during a severe streptococcic outbreak was accompanied by a precipitous, contraseasonal decline in streptococcic infections and was followed by a striking drop in the incidence of rheumatic fever.

EFFECT OF SULFADIAZINE PROPHYLAXIS INSTITUTED IN HALF A CAMP AT THE ONSET OF A SCARLET FEVER OUTBREAK

Camp 1 of a naval training station had served as an untreated control group for the prophylactic program during the early winter months of 1943-1944. The

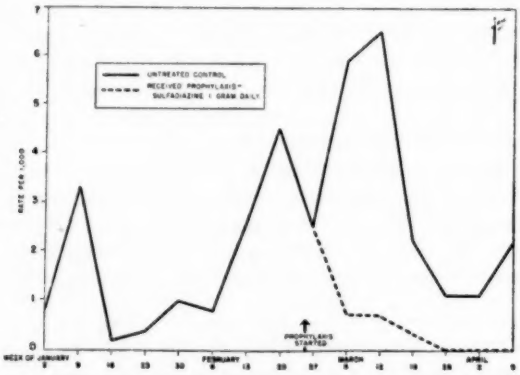

Chart 2.—The effectiveness of sulfadiazine prophylaxis as reflected by the incidence of scarlet fever in Camp 1 during the winter and spring months of 1944.

incidence of streptococcic infections among these 5,000 men had been moderate during December and January. About the middle of February the scarlet fever rate began to rise rapidly, and this was accompanied by a decided increase in the occurrence of other streptococcic respiratory diseases. Most of these infections, irrespective of the presence or absence of a scarlatinal rash, were caused by hemolytic streptococcus group A, type 19. On February 25 one half of the complement of this camp was placed on a prophylactic dose of 1 Gm. of sulfadiazine daily; the other half remained untreated. The effectiveness of sulfadiazine in preventing further

TABLE 4.—*Acute Respiratory Tract Infections* at Various Naval Activities in Chicago*

Admission Rates per Thousand Strength, Winter of 1943-1944

Naval Activity in Chicago	1943		1944			
	November	December	January	February	March	April
A	146	254	130	74	19	19
B	176	145	210	89	89	54
C	64	71	61	49	54	35
D	40	71	64	44	33	26
E	27	88	61	76	54	43
F	17	100	39	52	46	48

* Includes: tonsillitis, acute; pharyngitis, acute; catarrhal fever, acute; bronchitis, acute; laryngitis, acute; Vincent's angina; pneumonia, all forms; scarlet fever; septic sore throat; influenza; rheumatic fever.

spread of this highly communicable strain of hemolytic streptococcus in recruits receiving prophylaxis is shown in chart 2.

EFFECTIVENESS OF SULFADIAZINE IN PREVENTING IMPLANTATIONS OF HEMOLYTIC STREPTOCOCCUS IN A RECRUIT CAMP

The foregoing observations indicated that 1 Gm. of sulfadiazine administered daily was effective in checking a streptococcic outbreak, either when well advanced (Activity A) or in its early stage (Camp 1). The following observations will serve to show that as little as 0.5 Gm. of sulfadiazine administered daily prevents the implantation of the hemolytic streptococcus in a recruit group (Camp 2) with a complete turnover of personnel every four to six weeks.

Camp 2 was situated about 1 mile from Camp 1 on the same naval training station. In November 1943, when the incidence of streptococcic infections was low, this camp was divided into two groups for the purpose of this investigation. All even numbered companies were placed in group A, which received no chemo-

TABLE 5.—*The Incidence of Respiratory Infections (Probably Hemolytic Streptococcus) in Camp 2*

Four Week Period Ended	All Respiratory Illness with Positive Hemolytic Streptococcus Cultures					
	A. Control		B. Treated			
	Number Cases	Rate per 1,000	Number Cases	Rate per 1,000	x/σ	P
2/6/44	77	46.88	9	5.27	7.43	<0.0001
3/5/44	113	79.02	9	6.05	9.60	<0.0001
4/2/44	...	.....	18	6.88	....	.....

TABLE 6.—*The Incidence of Frank Streptococcic Infections in Camp 2*

Four Week Period Ended	Scarlet Fever, Tonsillitis and Pharyngitis					
	A. Control		B. Treated			
	Number Cases	Rate per 1,000	Number Cases	Rate per 1,000	x/σ	P
2/6/44	26	15.83	2	1.17	4.56	<0.0001
3/5/44	64	44.75	2	1.34	7.66	<0.0001
4/2/44	..	.....	3	1.15	....	.....

prophylaxis, and all odd numbered companies were placed in group B, which received 0.5 Gm. of sulfadiazine daily. On March 1 both groups were placed on a prophylactic regimen of sulfadiazine 1 Gm. daily. The incidence of respiratory symptoms and respiratory diseases of groups A and B is shown in chart 3. Data on the incidence of probable and frank hemolytic

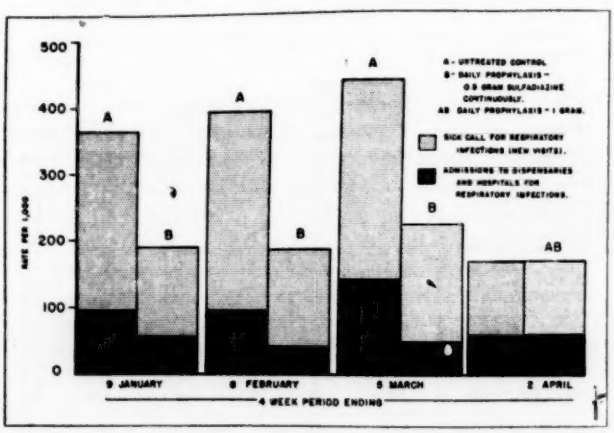

Chart 3.—The effectiveness of continuous sulfadiazine prophylaxis in preventing respiratory tract infections in Camp 2.

streptococcus infections of the two groups are summarized in tables 5 and 6.

It is seen in chart 3 and tables 5 and 6 that the group receiving sulfadiazine prophylaxis had a low incidence of respiratory infections. This low incidence in group B was maintained for three months, and perhaps greater protection was afforded during March, when the prophylactic daily dose of sulfadiazine was increased from 0.5 to 1.0 Gm. The incidence of sick call visits for respiratory symptoms in the untreated group was twice

that in the treated group, and the incidence of respiratory diseases requiring bed care in the untreated group was about three times that in the treated group. In both the difference in incidence between untreated and treated groups is statistically significant. This difference is even more striking for streptococcic infections. The incidence of respiratory disease probably caused by the hemolytic streptococcus in the untreated group was eleven times the incidence of the treated group. Frank streptococcic infections in the untreated group had an incidence twenty-four times that of the treated group.

EVALUATION OF THE POTENTIAL LIABILITIES AND ASSETS OF SULFADIAZINE PROPHYLAXIS

When this program was initiated, there appeared to be three potential dangers inherent in sulfadiazine prophylaxis: (*a*) sensitization of patients to sulfonamide compounds, (*b*) induction of severe, irreversible drug reactions, (*c*) development of drug fastness by respiratory pathogens.

Sensitization of Patients.—Mild evanescent dermal drug sensitization phenomena occurred in all three groups receiving sulfadiazine. The incidence of symptoms ascribed to the drug varied between 0.2 and 0.7

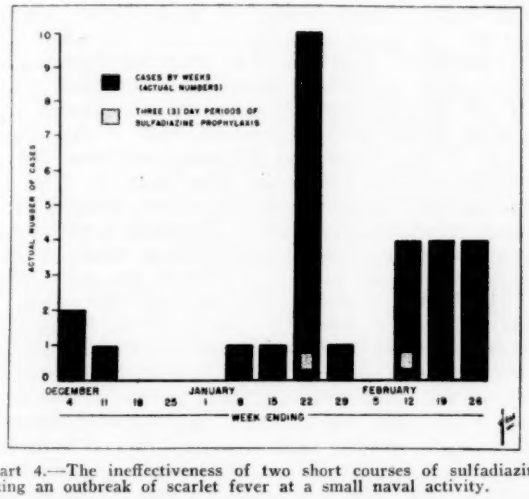

Chart 4.—The ineffectiveness of two short courses of sulfadiazine in checking an outbreak of scarlet fever at a small naval activity.

per cent. Approximately half of these reactors when retested had no drug symptoms and were replaced on the prophylactic program. The large majority of all reactions occurred in the second and third weeks of prophylaxis following the total dosage of 7 to 20 Gm. of sulfadiazine. The reinstitution of prophylaxis in groups who had been without sulfadiazine for a period of one to four weeks did not increase the incidence of drug reactions. A few individuals who had manifested sensitivity to sulfonamide compounds and who subsequently contracted severe respiratory infections were treated with penicillin. The collected findings indicated that a small percentage of persons have an idiosyncrasy to sulfonamide compounds administered in therapeutic or prophylactic doses and that sulfadiazine prophylaxis per se does not sensitize.

Severe Irreversible Drug Reactions.—Dangerous untoward reactions occurred in 0.01 per cent of individuals receiving sulfadiazine prophylaxis. These were of two types and about equally divided between exfoliative dermatitis and granulocytopenia. With supportive treatment these disease processes appeared reversible. The administration of therapeutic doses of sulfonamide to one man with a sulfonamide rash and bronchitis was followed by death. This was the only instance in which death occurred. The autopsy showed lymphadenopathy, which on microscopic examination proved to be leukemia.

Development of Drug Fastness by Respiratory Pathogens.—Fastness to sulfadiazine was apparently not initiated during the first four months of this prophylactic program. The evidence is:

1. There was no increase in the prevalence of any serologic type of hemolytic streptococcus in the groups on prophylaxis.
2. There was no increase in the proportion of hemolytic streptococci in the throat flora of individuals throughout the period of prophylaxis.
3. There was no increase in streptococcic morbidity throughout the period of prophylaxis.
4. There was no difficulty in obtaining a satisfactory therapeutic effect from sulfadiazine in individuals who contracted streptococcic infections while receiving prophylaxis.

In summary, the only liability incurred in this program was the development of a few severe drug reactions, 1 in 10,000 individuals receiving prophylaxis.

The gains from the program included prevention of disabilities, saving in man-days loss and a reduction in the costs for care of the sick and for pensions. The size of these gains was proportional to the incidence of bacterial infections of the respiratory tract. Among recruits with a high incidence of infections it was estimated that 343 man-days were saved per thousand weekly from bacterial infections. Most of these man-days were saved through the prevention of streptococcic infections. Since these infections are prone to cause debilitating sequelae, their prevention obviously created enormous benefits to Naval personnel and to the United States government in a state of war.

COMMENT

A number of observers have pointed out the effectiveness of a short course of sulfadiazine prophylaxis in checking outbreaks of meningococcic infections.[3] This measure not only breaks the epidemic process but also eliminates the meningococcus from the throat flora of carriers. Because of this a misconception has arisen in the handling of streptococcic outbreaks. Sulfadiazine, administered for a few days, either in prophylactic or in therapeutic doses, does not check a streptococcic outbreak and has little or no effect on the throat flora of individuals in the carrier state. This fact was demonstrated by a small naval activity experiencing an outbreak of scarlet fever. Sulfadiazine was given for three days in January with apparently good results; however, the outbreak recurred in February when another three day period of prophylaxis was administered with little effect. All personnel were subsequently placed on a continuous prophylactic program of sulfadiazine 1 Gm. daily, early in March. The streptococcic outbreak then subsided and only 2 new cases of scarlet fever occurred in the following ten weeks. The ineffectiveness of short courses of sulfadiazine at this activity is shown in chart 4. This experience illustrated that a three day course of prophylaxis, which will effectively check a meningococcic outbreak, is not adequate for preventing streptococcic infections The presence of sulfadiazine on the surface of mucous membranes prevents

3. Cheever, F. S.; Breese, B. B., and Upham, H. C.: The Treatment of Meningococcus Carriers with Sulfadiazine, Ann. Int. Med. **19:** 602-608 (Oct.) 1943. Thomas, H. M., Jr.: Meningococcic Meningitis and Septicemia: Report of Outbreak in Fourth Service Command During Winter and Spring of 1942-1943, J. A. M. A. **123:** 264-272 (Oct. 2) 1943. Kuhns, D. M.; Nelson, C. T.; Feldman, H. A., and Kuhn, L. R.: The Prophylactic Value of Sulfadiazine in the Control of Meningococcic Meningitis, ibid. **123:** 335-339 (Oct. 9) 1943.

implantation of hemolytic streptococci but does not modify the streptococcus flora already implanted.

The exact concentration of sulfadiazine in the nasopharyngeal secretions required to prevent implantation of bacterial respiratory pathogens is still unknown. In the course of the present studies it was found that individuals receiving a daily dose of 1 Gm. of sulfadiazine had blood values ranging between 2.6 and 1.7 with a median of 2.2 mg. per hundred cubic centimeters and that with a daily dose of 0.5 Gm. the blood values ranged between 1.8 and 0.8 with a median of 1.4 mg. per hundred cubic centimeters. The findings of others [4] have shown that the concentration of sulfadiazine in the secretions of the upper respiratory tract is about 60 per cent of blood levels. The observations made in Camp 2, therefore, indicate that these secretions containing less than 1 mg. of sulfadiazine per hundred cubic centimeters were adequate to prevent the implantation of most bacterial respiratory tract pathogens.

SUMMARY

1. The United States Navy is engaged in a long term program for the control of streptococcic infections and their disabling sequelae.

2. One component of this program involves mass prophylaxis with sulfadiazine.

3. Prophylactic doses of this drug were given continuously to about 250,000 naval trainees between December 1943 and April 1944.

4. This preliminary report deals with observations on only 30,000 men at three camps.

5. These observations indicate that the continuous ingestion of 1 Gm. of sulfadiazine daily is adequate (*a*) to check a well advanced streptococcic epidemic, (*b*) to check a streptococcic outbreak at its onset and (*c*) to protect 85 per cent of susceptible recruits from implantation with bacterial respiratory pathogens.

6. These observations also suggest that a continuous daily dose of 0.5 Gm. of sulfadiazine (affording a mean level of 1.4 mg. per hundred cubic centimeters in the blood and perhaps 0.8 mg. per hundred cubic centimeters in secretions of the respiratory tract) is almost 85 per cent effective in preventing implantation by Streptococcus haemolyticus.

7. The only untoward effect of mass sulfadiazine prophylaxis is the occurrence of evanescent rashes in 0.5 per cent and dangerous constitutional disturbances in 0.01 per cent.

8. Mass sulfadiazine prophylaxis is effective (*a*) in checking bacterial infections of the respiratory tract, (*b*) in preventing the development of disabling sequelae caused by these bacteria and (*c*) in aiding the economy of a nation at war.

ABSTRACT OF DISCUSSION

ON PAPERS OF COLONEL HOLBROOK AND COMMANDER COBURN

DR. T. DUCKETT JONES, Boston: I have no doubt that the general contentions of both speakers are absolutely true. There can be little doubt that sulfadiazine in dosages as indicated and administered as indicated will definitely affect the illness rates, particularly those caused by hemolytic streptococci. I do not think the question of sensitivity to these drugs is yet answered. Sensitivity may not develop until many months after the cessation of the preventive administrations. That is a serious problem, and I wonder if either speaker had any means whereby he might evaluate the question of development of sensitivity in any of the men receiving the drug. Commander Coburn showed some stations that were control stations. In my experience there have been great differences in illnesses, so that this type of control must be difficult. Neither presentation showed bacteriologic charts, but apparently the charts included bacteriologic infections. The only data at present with regard to rheumatic fever are those of Colonel Holbrook, and I saw no significant difference in the group as he presented it. In conclusion I should like to suggest that perhaps we may control the major features of streptococcic illness by giving the drug to small groups of men who constitute a single epidemiologic unit and base conclusions on the actual illness experiences in these groups. We know that at least 50 per cent of the men will not need preventive measures. It is possible that the drug can be used intelligently to prevent the maximum amount of disease by giving the drug to the minimum number of men.

CAPTAIN RICHARD G. HODGES, M. C., A. U. S.: In evaluating an epidemiologic experiment on respiratory disease it is necessary to exercise considerable caution because there are a number of factors which can cause considerable variation in the respiratory disease rates. In the military population the seasoning of the troops is extremely important. The living conditions of the troops, particularly as pertain to ventilation and dust, the duties of the troops and finally the inflow of new material into the population may also cause profound changes. It is possible that the mass of Commander Coburn's material makes careful control of these factors somewhat unnecessary. However, to substantiate his contentions I should like to mention my experience at an Army Air Force technical school where a considerable degree of control was possible. The school was almost ideally set up for a controlled experiment, being divided into two teaching shifts of approximately 5,000 men each. The duties, the living conditions and even the recreations of the two groups were identical. They were on different time schedules, and thus mixing between the two was at a minimum. Percentage distributions according to length of stay on the field, according to the length of service and according to age were approximately the same for the two. The inflow of new troops into these two groups was approximately equal. Finally, for the preceding fifteen months component squadrons of the school were found to have behaved similarly toward respiratory disease and to an approximately similar degree. During January both groups showed a progressive rise in rate. On the 2d, 3d and 4th of February the members of one teaching shift received 2 Gm. of sulfadiazine per day. Their rate dropped sharply, while the control group's continued to rise. The drop lasted ten days. Then the other group was placed on 2 Gm. a day for two days and showed a corresponding but somewhat less prolonged response. Finally one group was placed on a continuous dosage of 1 Gm. a day and the other group was placed on 2 Gm. a day for two days, and then that was repeated one week later. Both dropped sharply. The response was greatest in streptococcic infections. The streptococcus disease rate was lowered almost to zero by each administration. Thus I believe that the effectiveness of the treatment with sulfadiazine is established.

COMMANDER ALVIN F. COBURN (MC), U.S.N.R.: There are two points that I should like to mention before the conclusion of this discussion. One is that conditions in naval training camps lend themselves well to controlled studies. Alternate companies can either be given prophylaxis or serve as untreated groups. Accurate data can be obtained. Except for the one program which, as I stated, was instituted during an epidemic at a naval activity here in Chicago, all of the navy studies were controlled. Companies selected in random fashion mingled and slept in the same barracks, used common mess halls and exercised together in common drill halls. These studies in the effectiveness of chemoprophylaxis were made under ideal conditions. The second point, which was mentioned only briefly, is that sulfadiazine prophylaxis was effective in preventing rheumatic fever. The incidence of rheumatic fever among men receiving chemoprophylaxis was 15 per cent of the incidence in control groups. Approximately 85 per cent of the expected rheumatic fever cases appeared to be eliminated by sulfadiazine.

4. Norris, C. M.: Sulfonamides in Bronchial Secretion: The Effect of Sulfonamides in Bronchiectasis, J. A. M. A. **123**: 667-670 (Nov. 13) 1943.

DR. ROY W. SCOTT, Cleveland: Are there any advantages of sulfadiazine over sulfathiazole?

COLONEL W. PAUL HOLBROOK, M. C., A. U. S.: Dr. Jones asked about what is being done to determine the question of sensitivity. The possibility of individuals becoming sensitized to the drug has been considered. As yet, evidence for an increasing sensitivity in individuals who are on the prophylactic program is not available. Repeated periods of prophylaxis on the same groups have shown in each instance a decreased number of reactors for the second or third prophylactic period rather than an increase. Once the known positive reactors are eliminated, no further difficulty is encountered during subsequent periods of prophylaxis. We also now have a rather large number of troops who have had prophylactic sulfadiazine and who have subsequently developed an acute illness requiring the administration of sulfadiazine therapeutically. These patients have responded as well as those not having had a prophylactic period. These experiences do not appear compatible with an increasing sensitivity. A long range study is planned by means of recording each individual's prophylactic record on his immunization register, so that in six months or a year a rather large accumulation of information should be available on this subject. I have not used sulfathiazole, largely because of the general reports in the literature as to its increased toxicity, but I have no experience in its use for this type of prophylaxis.

THE TREATMENT OF TONSILLITIS WITH SMALL DOSES OF SULFONAMIDES

CAPTAIN EDWARD D. FREIS
MEDICAL CORPS, ARMY OF THE UNITED STATES

From both military and economic aspects, any relatively nontoxic therapy which will shorten the course of a prevalent disease, if even for a few days, is worthy of application. Since it is generally acknowledged that tonsillitis is responsible for a significant number of the total man hours lost to industry and the armed forces, the advisability of treating acute follicular tonsillitis with sulfonamides has been the subject of a variety of studies. From the medical point of view, chemotherapy would be desirable because of the possibility that such complications as peritonsillar abscess and such sequelae of tonsillitis as nephritis and rheumatic fever might be prevented or at least minimized.

The advisability of using large doses of sulfonamides (2 Gm. or more per day) in the treatment of tonsillitis remains controversial. Some believe that, since this disease is relatively benign and self limited, chemotherapy is unnecessary and even dangerous.[1] This view is supported by the number of serious toxic reactions that have resulted from the indiscriminate use of the sulfonamides. Others believe with Gettelman and Kaiz [2] that early treatment with sulfonamides (2 Gm. per day) appreciably shortens the course of the disease. A middle of the road point of view is taken by Janeway,[3] who prescribes chemotherapy only for those patients whose temperature exceeds 102 F.

In addition to systemic therapy, the local treatment with sulfonamide sprays has become popular. Many investigators have reported effective therapeutic results and an absence of drug reactions following the use of local sprays in the treatment of various upper respiratory infections.[4]

In order to establish the relative efficacy of the local and systemic administration of sulfonamides in the treatment of acute follicular tonsillitis we considered it necessary to study this question under controlled conditions using hospitalized patients.

METHOD

During the winters of 1943 and 1944 a series of 405 young men of military age who had definite clinical evidence of acute follicular tonsillitis were hospitalized to a separate ward devoted to their care. During the first year of the study the patients were divided into two groups, alternate patients being treated by one of two methods. One group (1) of 100 patients were given only hot saline irrigations every four hours and received no chemotherapy. The other group (2) of 100 patients were treated with hot saline irrigations every four hours and in addition received sulfanilamide spray to the tonsils and pharynx every two hours except while asleep. Powdered sulfanilamide was sprayed into the throat until an even white coating of the mucous membranes was produced, the patient being then instructed to swallow, following which the throat was again sprayed.[5] The amount of sulfanilamide used per dose varied from 75 to 100 mg. and, as eight applications were administered daily, the total daily dosage varied from 500 to 800 mg. With this dosage blood sulfanilamide levels were never found to be above 1 mg. per hundred cubic centimeters and usually were too low to be read by standard methods.

During the second year group 3, consisting of 115 patients, received saline irrigations every four hours and, in addition, 125 mg. of sulfadiazine by mouth four times a day (500 mg. daily). The sulfadiazine was in tablet form and was swallowed immediately. Another group (4) of 90 cases was treated in the same way as group 2 except that "micraform crystals" of sulfadiazine [6] were substituted for sulfanilamide powder.

On admission a throat culture and white blood count were obtained. Patients who showed peritonsillar abscess, fusospirochetal ulcers of the tonsil, scarlet fever, acute glomerulonephritis or rheumatic fever on admission were not included in this study. Similarly excluded were patients who had the common cold with nasopharyngitis and tonsillar swelling without pronounced redness or follicles.

As indicated in the table, the four groups were essentially similar in regard to admission temperature, infecting organism and average admission leukocyte counts.

From the AAF Rheumatic Fever and Streptococcal Disease Control Program.

Lieut. Col. Robert King, M. C., and Dr. Chester S. Keefer cooperated with suggestions and criticisms.

From the Medical and Laboratory Services, AAF Regional Station Hospital, U. S. Army Air Field, Lincoln, Neb.

1. Rhoads, P. S., and Afremow, M. I.: Sulfanilamide in the Treatment of Sore Throat Due to Hemolytic Streptococci, with Controls, J. A. M. A. **114:** 942 (March 16) 1940. Richards, L. G.: Treatment of Diseases of the Throat, ibid. **115:** 501 (Aug. 17) 1940. Hughes, L. W.: Diseases of the Nasopharynx, Mississippi Doctor **18:** 261 (Oct.) 1940. Kernan, J. D.: Infections of the Mouth, Pharynx, and Respiratory Tract, Bull. New York Acad. Med. **17:** 674 (Sept.) 1941. Beckman, H.: Treatment in General Practice, ed. 4, Philadelphia, W. B. Saunders Company, 1942.

2. Gettelman, E., and Kaiz, S. P.: The Treatment of Severe Tonsillitis in a Naval Dispensary, U. S. Nav. M. Bull. **42:** 399 (Feb.) 1944.

3. Janeway, C. A.: Medical Progress: The Sulfonamides, New England J. Med. **227:** 1029 (Dec. 31) 1942.

4. Freeman, M. S.: Local Use of Sulfathiazole Powder for Acute Pharyngeal Infections, Arch. Otolaryng. **37:** 496 (April) 1943. Silcox, L. E., and Schenck, H. P.: Use in Otolaryngology of Microcrystals of Drugs of the Sulfanilamide Group, ibid. **36:** 171 (Aug.) 1942. Dolowitz, D. A.; Loch, W. E.; Haines, H. L.; Ward, A. T., and Pickrell, K. L.: The Prevention of Ear and Nasal Sinus Complications of the Common Cold, J. A. M. A. **123:** 534 (Oct. 30) 1943. Turnbull, F. M.; Hamilton, W. F.; Simon, E., and George, M. F.: Sinusitis and Infections Secondary to the Common Cold, ibid. **123:** 536 (Oct. 30) 1943.

5. The DeVilbiss standard atomizer-type powder blower No. 175 was used.

6. Smith, Kline and French laboratories supplied the sulfadiazine micraform crystals.

RESULTS

The groups which received sulfonamides (2, 3 and 4) either locally or systemically showed a return to normal temperature and "clinical recovery" in an appreciably shorter period of time than the control group (1) treated with irrigations alone (as shown in the table). Statistical examination of our data reveals that a reliable difference exists between group 1 and the other (sulfonamide treated) groups, since the reliability of the differences of the control group as compared with each of the sulfonamide treated groups is greater than three.

The criteria for "clinical recovery" were complete subjective relief of symptoms and complete disappearance of erythema, edema and follicles. Many of the patients, particularly in the sulfonamide treated groups, were subjectively well before the signs of inflammation had completely subsided. Hence it is probable that in other hands this period of "to clinical recovery" might be shorter or longer. Obviously this interim has not the same objectivity as "return to normal temperature" and therefore is not equally significant.

Summary of Data

Groups	No. of Cases	Temperature on Admission	White Blood Cells on Admission, Thousands	Positive Hemolytic Streptococcus	Days to Normal Temperature				Days to Clinical Recovery				Complicating Peritonsillar Abscess
					Mean	S. D.	S. E. M.	Reliability of Difference	Mean	S. D.	S. E. M.	Reliability of Difference	
1	100	101.6 (98.8-104.2)	13.7 (5-24)	83	3.3	1.68	0.168	...	4.7	1.95	0.195	...	6
2	100	101.7 (98.6-104.6)	13.6 (5-23)	85	2.3	1.07	0.107	5.0	3.5	1.44	0.144	5.0	1
3	115	101.7 (99.2-104.8)	12.5 (5-23)	86	1.6	0.88	0.082	9.1	3.6	1.24	0.116	4.9	1
4	90	101.4 (98.6-104.5)	12.6 (5-26)	78	1.4	0.73	0.077	10.2	3.0	1.15	0.121	7.4	0

S. D. (standard deviation) $= \sqrt{\frac{\Sigma d^2}{n}}$

S. E. M. (standard error of mean) $= \text{S. D.}/\sqrt{n}$.

Reliability of difference $= \frac{\text{Difference between means}}{\sqrt{(\text{S. E. M.}_1)^2 + (\text{S. E. M.}_2)^2}}$ (all comparisons made between group 1 and the other groups).

The control group (1) showed an incidence of 6 cases of peritonsillar abscess, which developed as a complication during the period of hospitalization. In both the sulfanilamide spray treated group (2) and in the group receiving sulfadiazine tablets (3) one complicating peritonsillar abscess developed, while none occurred in the group receiving micraform crystals of sulfadiazine as a local spray.

The data reveal that the temperature returned to normal more rapidly in the sulfadiazine treated groups (3 and 4) than in the sulfanilamide spray treated group (2). The group receiving sulfadiazine micraform crystals locally (4) seemed to be the most benefited. However, the differences between the various sulfonamide treated groups are not of sufficient significance to merit separate discussion.

None of the patients who received sulfonamides developed either toxic reactions or evidences of sensitization.

COMMENT

Our data demonstrate that small, nontoxic doses of sulfonamides will appreciably reduce the period of illness associated with tonsillitis, irrespective of the route of administration of the drug. That the difference between the sulfonamide treated groups and the control group is real is indicated by statistical examination of the data. The small difference between groups 3 and 4 and group 2 can be attributed to the well known fact that sulfadiazine is more effective in infections caused by the hemolytic streptococcus than is sulfanilamide.

The fact that the patients in group 3, who received 0.5 Gm. of sulfadiazine daily in tablet form, showed a rate of recovery comparable to the groups receiving local spray raises the question of the advisability of using topical therapy in the treatment of tonsillitis. As tablets are more easily administered than local spray, there is no clinical reason for the use of the latter in the treatment of this condition.

The saving of even one day in hospitalization has much economic and military importance, since, when the incidence of tonsillitis is considered, this saving can be translated into terms of thousands of man-days salvaged. In view of the fact that the patients receiving sulfonamides experienced subjective relief even though some residual signs of subsiding inflammation remained, it is possible that such patients can be discharged to military duty or to industry as soon as the temperature becomes normal, with the stipulation that they continue to take small doses of sulfadiazine for several days thereafter. A further saving of time would thereby result.

It is possible that the use of more than 500 mg. of sulfadiazine daily would have further hastened recovery. However, when dealing with a potentially harmful drug, a balance must be struck between effective and toxic dosage. The complete absence of sulfonamide reactions in the treated groups favors the use of small dosage in the treatment of tonsillitis. This does not imply that these small doses of sulfonamides necessarily are effective in other infections.

CONCLUSIONS

1. The administration of small doses of sulfonamides appreciably shortens the course of acute follicular tonsillitis and minimizes the complication of peritonsillar abscess.

2. Small doses (500 mg. per day) of sulfadiazine administered by mouth in tablet form are as effective as the local application of sulfonamides to the tonsillar area in the form of a powder spray. The ease of administration makes the systemic route the ideal therapeutic procedure.

3. There were no toxic or sensitization reactions observed in any of the 305 patients receiving sulfonamides in the doses given.

Clinical Notes, Suggestions and New Instruments

HEMOGLOBIN ESTIMATION BY THE REVOLUTIONARY COLORIMETRIC METHOD OF KENNEDY

WITH FURTHER REPORT ON A SIMPLE INSTRUMENT FOR FACILITATING THE UTILIZATION OF THE PRINCIPLE

DON H. DUFFIE, M.D., CENTRAL LAKE, MICH.

In 1926 Robert P. Kennedy[1] published a method of colorimetry, for hemoglobin especially, that was so new, so valuable, that it is indeed regrettable that the very scholarliness of his paper seems to have concealed his discovery from most of us.

With the exception of spectrophotometry, practically all previous colorimetry had comprised sundry expedients for the matching of colors. In Kennedy's hemoglobin method, by means of a light filter transmitting such a narrow band of wavelengths in the green as to be virtually monochromatic, he simply eliminated color from both standard and unknown, then matched light intensities instead—a totally different concept.[2] He could do this—and this is the whole point—because, as seen through his filter, red and gray both appear green. Not merely green, but when illuminated to equal brightness both appear of the identical hue of green.

I have stated before[3] the basic principle as applied to hemoglobin, that green light is absorbed by a red solution. The more red substance present, the less green light will get through, so that by suitably measuring how much does get through the amount of the red substance (oxyhemoglobin) may be computed.

As Kennedy points out, color filters had been employed in colorimetry as far back as Leonardo da Vinci in the sixteenth century, but to the best of my knowledge always either as a means of facilitating color matching or else in the absurd quest of finding an exact additive color complement for each and any color, so that the combination might then be compared in intensity with white light.

The bold idea of cutting loose from color entirely, of doing with our own eyes exactly what the photoelectric colorimeter does—quantitative measurement of colored light—that, so it is believed, was new with Kennedy. In spite of his superb work, however, said photoelectrics have right to date enjoyed virtual if quite unwarranted monopoly of the principle. Kennedy's hemoglobin method does sound cumbersome: indeed it was never propounded as a clinical method, though it may readily be adapted as such very satisfactorily.[4]

Unaware of Kennedy's work until it was brought to my attention by another[5] who found himself inadvertently trespassing on Kennedy's domain, I, a country doctor and reformed color process photoengraver, had arrived at the same idea empirically, thanks to years of familiarity with light filters in the trade. Kennedy used an ordinary colorimeter, a number 74 filter, one cup replaced by a fixed gray standard, the solution depth in the other cup varied as needed to secure a luminosity match with the gray standard. I applied the principle in reverse, keeping the solution layer constant and securing a match by varying the gray, in the form of an optical wedge. This application lends itself to a less elaborate instrument, a less expensive one, and one considerably quicker to use. The scale, for direct reading through the eyepiece, is superimposed on the margin of the wedge. This instrument that I have devised is a plungerless, one cup colorimeter (more correctly, photometer) using a micrometer measured Kahn vial for solution cup and having my own green filter incorporated in the eyepiece. One time saving feature of this construction when used for hemoglobin is that, while a precise 20 cu. mm. of blood must be used, the volume of diluent need not be measured at all. This is because light reaching the eye vertically through the solution will have encountered a constant quantity of blood per unit area, be the depth little or much. (It is ever a disappointment when any one fails to argue this point!) The test can readily be done in less than one minute.

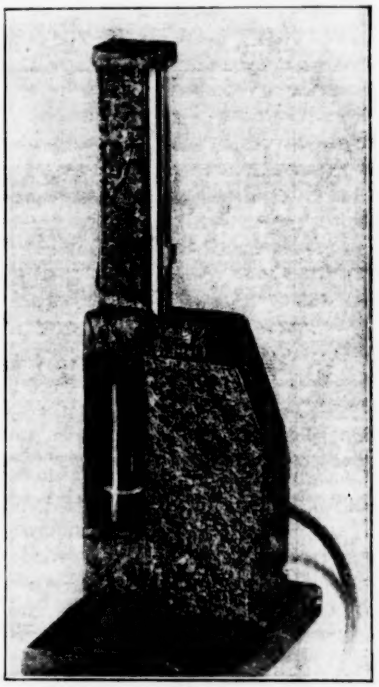

Fig. 1.—Simple photometer employing Kennedy's principle. Fields are matched by manipulation of an optical wedge moving in the sleeve at right of ocular. Scale is read through the eyepiece.

CALIBRATION

Aware of having neither ability nor facilities for the quest of the absolute in hemoglobin values, I am content, in calibrating my instrument, to strike a compromise among the weird choas of calibration levels of instruments already on the market, in which discrepancies of more than 3 grams are found! Since in this type of instrument there are economic and other objections to continuing the wedge down to zero, mine has been arbitrarily restricted to the range between 5 and 20 Gm. of hemoglobin. For zero set, readings are made from a sheet of permanent gray standard, and, in event of the gray not giving a match at the supposed value, the lamp of the instrument is adjusted in position until it does. One advantage of such an arrangement is that it gives free rein to individual convictions in the matter of calibration levels, which may be "remodeled to suit tenant" in a moment. The critic need but set the instrument scale to read whatever his own oracle decrees the blood in question should read and then adjust the lamp position, if need be, until it does. The gray standard is then read at the new setting and labeled accordingly. Stability is thus assured until another Pharaoh arises! This permanent gray standard may be either an Eastman neutral density filter in glass, density 1.0, two layers of fine monel or other screen in glass as suggested by Sunderman,[5] or my present preference, a small square of engraver's halftone screen.

ACCURACY

Karr and Clark,[6] in hundreds of determinations by several of the commoner hemoglobin methods, after applying all corrections found fewer than one half of the readings to be within

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The instrument is not in commercial production "for the duration." A few of the instruments are being built in the author's hobby shop.

1. Kennedy, R. P.: The Use of Light Filters in Colorimetry, with a Method for the Estimation of Hemoglobin, Am. J. Physiol. **78:** 56 (Sept.) 1926.

2. Should any suspect this to be distinction without difference, let him ponder the unequal scale divisions, so much farther apart in the lower concentrations, of any hemoglobin instrument employing the wedge principle on a color matching basis. Contrast this with the scale divisions in equal parts throughout, where the wedge is used on the Kennedy principle, as in my own photometer.

3. Duffie, D. H.: The Elimination of Color from Visual Hemoglobinometry, J. A. M. A. **119:** 493 (June 6) 1942.

4. But meager outline may be given here. A colorimeter cup not more than 12 mm. in diameter is preferable. A piece of Eastman neutral density filter of density 0.5 mounted in glass replaces one colorimeter cup. If brilliant illumination is available, Wratten number 74 filter is laid over the eyepiece; if not, one layer of number 15 and two layers of number 60 film filter. (For some eyes one layer of 60 is enough to exclude all red.) In the remaining colorimeter cup 0.02 cc. of blood (Sahli pipet) in 5 cc. of 0.4 per cent ammonium hydroxide solution is placed and the fields are matched. My own experience with such an instrument is too scanty for dogmatism, but by trial with known blood dilutions a factor may be worked out which, divided by plunger height (decimal point appropriately inserted) will give the hemoglobin in grams per hundred cubic centimeters. The factor 1.7 is believed to be not greatly in error. Once a table or curve for direct reading of results is prepared, the method is rapid.

5. Sunderman, F. W.: Personal communication to the author.

6. Karr, W. G., and Clark, J. H.: Comparison of Various Hemoglobin Methods as Performed in Hospital and Physicians' Laboratories, Am. J. Clin. Path. (Tech. Supp.) **5:** 127 (Sept.) 1941.

0.5 Gm. (3 per cent) of the mean. In a test later reported by one of them [7] on my instrument, in which two of the three observers had had no practice, 95 per cent of the sixty readings were within 0.25 Gm. of the mean (1.5 per cent). This is indeed a precision often unattained by the photoelectrics.

The secret of this higher precision is believed to lie in the filter employed. The retina evidently has heightened sensitivity to minute differences in intensity for wavelengths transmitted by this filter when shielded from the "glare" of waves excluded by the filter's absorption.

BLOOD CHEMISTRY

Not knowing (fortunately) that maximum filter transmission theoretically should be restricted to a wavelength range coinciding with the maximum absorption of the solution to be tested, so that a different colored filter would be required for nearly every color of solution measured, I went ahead, using my same green filter for all the blood chemistry filtrates I could find. Before learning from wiser heads that this could not be done, I had done it. Entirely satisfactory readings were obtained, which plotted as almost straight lines, from

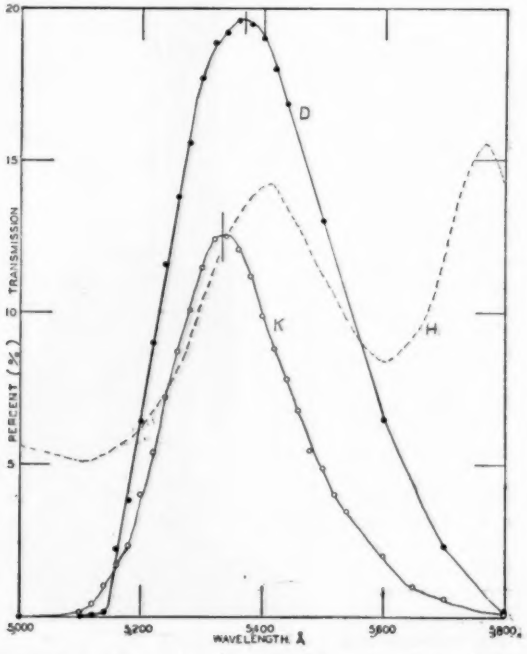

Fig. 2.—Transmission curves of Kennedy's filter (*K*), Duffie (*D*), shown against the absorption curve of oxyhemoglobin.

blood sugar, creatinine, urea, phosphorus, tyrosine, total protein, Haslam's [8] unpublished serum protein method, nonprotein nitrogen and all modifications tried of the Bratton-Marshall sulfa-concentration method. The case with creatinine is interesting. The filtrate itself gives perfectly sharp readings, whereas the bichromate standards, indistinguishable to the eye from the respective filtrates, give no readings whatever with this filter. It was to me surprising that the greens of the blood cholesterol test can also be closely read through the green filter, though they plot a sharply inflected curve. While it is true that with one or two of these solutions this filter does not give an absolute hue match, even so, the only blood chemistry test I have found on which it will not give satisfactory readings is the yellow of the sulfonamide concentration test with Ehrlich's reagent. The saving of the technician's time is obvious if standard solutions need be run but once for calibration then occasionally as check on reagents.

7. Karr, W. G.: Personal communication to the author in October 1942.

8. Haslam, T. P.: Personal communication to the author. (According to Haslam's equation, if for blood sugar precisely 3 cc. of the filtrate is used in my instrument, a cipher added to the gram scale reading gives the sugar in milligrams per hundred cubic centimeters.)

CALIBRATION FOR OTHER TESTS

Once a set of four or five standard solutions have been processed, in strengths covering the usual clinical range of the test, calibration is almost quicker done than fully described. Briefly, readings are obtained in the instrument from suitable and precisely equal volumes of these standard solutions, plotted on graph paper against the known concentrations of these solutions, and a standard curve drawn. Valúes of identical volumes of unknown solutions may then be instantly evaluated in terms of concentration, from the curve. Having done which, one may be reasonably sure of his results and need take no man's word for anything.

SULFONAMIDE CONCENTRATION TESTS

Readings of sulfonamide drug concentration tests by any method using Marshall's reagent may be done so accurately on this instrument, with the same filter and from such small amounts of blood, that truly micro volumes may be used, 0.02 cc. of blood instead of 0.2-0.3 cc., as in several micro methods.

TWO CASES OF CLOSTRIDIUM WELCHI INFECTION TREATED WITH PENICILLIN

MAXWELL KEPL, M.D.; ALTON OCHSNER, M.D., AND J. LEONARD DIXON, M.D., NEW ORLEANS

We believe that the development of gas gangrene in a traumatic wound depends on four factors: (1) contamination of the wound with soil or foreign bodies containing clostridia, (2) inadequate blood supply to the affected part, (3) inadequate débridement and (4) conditions in the wound for anaerobic growth. A combination of these four factors in a given patient will almost invariably give rise to clinical "gas gangrene."

Once clinical "gas gangrene" has fully developed, the only known treatment is radical surgery, laying the affected parts wide open and many times, of necessity, doing a high guillotine amputation in order to save the patient's life.

Any chemical or biotic substance which will inhibit the growth of clostridia in traumatic wounds would be of inestimable value in saving limbs and lives.

The discovery by Fleming [1] of the action of penicillin and its use by McIntosh and Selbie [2] in experimental Clostridium welchi infections held promise that this drug would be of value in such infections. As animal experiments are inconclusive in regard to human therapy, it remains for the clinician to put penicillin to the final test in regard to its efficacy in the treatment of gas gangrene. The recent report of Keefer, Blake, Marshall, Lockwood and Wood [3] indicates that more clinical observation on the action of penicillin in "gas gangrene" infection is needed in human cases before definite conclusions can be drawn. Lyons [4] also makes a similar plea.

McKnight, Loewenberg and Wright [5] have reported their experience in a case of "gas gangrene." They could not control the "gas gangrene" infection with wide incisions, sulfathiazole systemically, large doses of gas antitoxin and high voltage x-ray therapy. A high arm amputation was resorted to, but

Leah Seidman Shaffer, ScD., made the bacteriologic studies.

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Dr. Kepl is fellow in orthopedic surgery, Division of Medical Sciences, National Research Council.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Tulane University of Louisiana.

1. Fleming, A.: An Antibacterial Action of Cultures of Penicillin with Special Reference to Their Use in Isolation of B. Influenzae, Brit. J. Exper. Path. **10:** 226 (June) 1929.

2. McIntosh, J., and Selbie, F. R.: Zinc Peroxide, Proflavine and Penicillin in Experimental Cl. Welchii Infections, Lancet **2:** 750 (Dec. 26) 1942.

3. Keefer, C. S.; Blake, F. G.; Marshall, E. K., Jr.; Lockwood, J. S., and Wood, W. B., Jr.: Penicillin in Treatment of Infections, J. A. M. A. **122:** 1217 (Aug. 28) 1943.

4. Lyons, C.: Penicillin in Surgical Infections in the United States Army, J. A. M. A. **123:** 1007 (Dec. 18) 1943.

5. McKnight, W. B.; Loewenberg, R. D., and Wright, V. L.: Penicillin in Gas Gangrene, J. A. M. A. **124:** 360 (Feb. 5) 1944.

gas bubbles persisted in the axillary wound. Intravenous sodium penicillin in isotonic solution of sodium chloride was given continuously on the second postoperative day until the edematous condition of the patient made it necessary to stop therapy. In addition, the patient received 40,000 units directly intramuscularly into the stump. During the next week the temperature gradually dropped, and the wound cleaned up. No positive bacteriologic identification of the causative organism was done, owing to inadequate laboratory facilities. It was agreed by four experienced clinicians, however, that the case was one of clinical "gas gangrene."

Recently we have had occasion to study two cases of Clostridium welchi infection, both of which were treated with penicillin. In one, following a shotgun injury to the lateral aspect of the thigh, there was no evidence of clinical "gas gangrene," but a persistent Cl. welchi cellulitis associated with Staphylococcus aurantiacus, coagulase positive, and a gram negative anaerobic bacillus, unidentified as yet. Calcium penicillin was applied directly to the wound in a dilution of 5 cc. of isotonic solution of sodium chloride containing 20,000 units. Local administration of this dosage was continued for six days. Cultures were taken before, during and after penicillin therapy. Under local penicillin therapy the number of gram negative organisms and Staphylococcus aurantiacus appeared reduced in direct smear preparation with an increase in the number of

Fig. 1.—Arm and forearm, edematous, "wet" and ischemic before penicillin and surgery. Note the multiple bullae.

cocci phagocytized. The clostridia found lacked a good capsule but persisted undiminished in the wound throughout penicillin therapy. A milk tube inoculated with a swab consistently showed "stormy" fermentation. The wound healed slowly by granulation over a period of seven weeks, and at no time was the patient's general condition impaired by the Cl. welchi cellulitis.

The second case was that of a man whose arm was lacerated by broken glass which severed the biceps, the brachialis, the radiobrachialis muscles, the brachial artery, the radial and median nerves and the median basilic vein. Bleeding was severe, and a tight tourniquet was put on before he entered the hospital. Complete débridement and closure were done early, followed by repeated stellate blocks and packing of the injured extremity in ice. The temperature, 100 F. on admission, went to 102 F. the next day. The fingertips were inspected at that time and found warm and pink. The patient began to complain of severe pain in the arm. On the third day the arm was swollen and painful to the touch. Dressing on the fourth day revealed crepitation along the radial side of the forearm, with bubbles of gas escaping from the suture line. There was bronzing of the tissues around the elbow and a putrefactive odor to the arm. Multiple bullae were present on the skin of the forearm. The fingertips were cold and pale (fig. 1). The patient was toxic and in great pain, with a temperature of 103 F.

All sutures were removed, smears of exudate made and a blood culture was taken. Cl. welchi and beta-hemolytic streptococci were identified from the wound, and blood culture was positive for beta-hemolytic streptococci. Sulfadiazine was immediately given by mouth, 70,000 units of "gas gangrene antitoxin" given intramuscularly, hot wet dressings applied locally, and a transfusion of 500 cc. of citrated blood administered. The next morning the temperature had dropped a little, he appeared less toxic, and his blood culture had become negative. His arm had definitely become worse, however, and the edema appeared to have spread to the axilla, while crepitation could be noticed in the upper arm and shoulder. One hundred thousand units of sodium

Fig. 2.—Appearance of stump the day after surgery and penicillin. The gloved finger is placed in the lateral skin flap. The exposed biceps muscle is viable.

penicillin was given in 100 cc. of isotonic solution of sodium chloride intravenously, 500 cc. of citrated blood was given and a guillotine amputation was done under cyclopropane anesthesia. At operation, the skin and fascia of the stump were split longitudinally and left open. Swabs taken from this area at operation showed gram positive bacilli and gram positive cocci, which on culture proved to be Cl. welchi and beta-hemolytic streptococci. Powdered calcium penicillin, 100,000 units, was sprinkled dry into the stump, Dakin tubes were inserted, the stump was bandaged and sealed with cellophane, and a continuous local drip of 1,000 cc. of isotonic solution of sodium chloride containing 100,000 units of calcium penicillin started.

The next morning the wound was dressed. The exposed muscle was clean. A culture taken from the wound showed only a scant growth of diphtheroid organisms. No Cl. welchi or beta-hemolytic streptococci were found (fig. 2) on smear or culture.

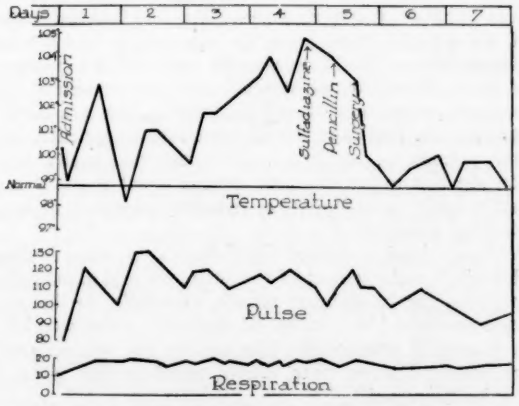

Fig. 3.—Temperature, pulse and respiration during the first week in the hospital. Notice the sharp drop in temperature and pulse rate following penicillin and amputation.

The clinical course postoperatively was uneventful except that a thrombophlebitis developed at the site of the intravenous penicillin therapy. The stump now has a pyocyaneus infection from ward contamination, but healing is assured. The patient still has a low fever, 99 F., but the stump is ready for skin grafting. Figure 3 shows the temperature, pulse and respiration curves during the first week in the hospital.

SUMMARY

Of 2 cases of Cl. welchi infection, 1 was treated locally with calcium penicillin and the other systemically with sodium penicillin and locally with calcium penicillin. Careful bacteriologic studies showed persistence of Cl. welchi in the case of cellulitis treated with calcium penicillin locally, while the use of penicillin systemically and locally, combined with guillotine amputation, caused the disappearance of beta-hemolytic streptococcus and Cl. welchi from the spreading infection. After oral sulfadiazine, beta-hemolytic streptococci could not be recovered from the blood stream. It must be emphasized that good surgery was the deciding factor in the second case and that penicillin is of most benefit when used in conjunction with good surgical principles.

A PRIMIPARA WITH DIABETES AND MILD TOXEMIA TREATED SUCCESSFULLY WITH DIETHYLSTILBESTROL

BYRON D. BOWEN, M.D., BUFFALO

The wide experience of Priscilla White[1] in the study of the chorionic gonadotropic hormones and the effect of the use of the estrogens and progesterone in the treatment of pregnant diabetic patients, on whom an increase of these hormones was found, is more than suggestive that their use reduces the incidence of, and is effective in, the treatment of preeclamptic toxemia of pregnancy and thereby reduces the fetal and maternal mortality.

The nature of this action is not understood, nor is the metabolism of the estrogens. It may be that the estrogenic substances have a "salutary" effect on the liver. It has been demonstrated that pregnant women can tolerate large amounts of estrogens. Among the possibilities of this beneficial effect are the inhibition of the diabetogenic hormones of the pituitary, the reduction of the rate of glycogenolysis or the removal of antagonistic insulin action, as White's cases have shown that insulin could usually be reduced after the administration of the estrogen. The following case demonstrates this relationship to a high degree:

REPORT OF CASE

History.—Mrs. E. F., aged 23, admitted to the diabetic service of the Buffalo General Hospital Oct. 7, 1943 and discharged Jan. 9, 1944, was referred by Dr. Raymond May, Alden, N. Y. The diabetes was discovered in 1932; she had taken insulin since that time. Because of considerable variation in weight and insulin dosage it was suspected that the control of the diabetes had not been accurate much of this time. She had been in various hospitals on several occasions for adjustment of the diabetic regimen. One of these admissions, at the age of 15, was because of diabetic coma. She had had an enlargement of the thyroid gland since the age of 10. At the time of admission the insulin dose was 90 units of the protamine zinc and 10 to 20 units of the unmodified before breakfast. Her last menstrual period was March 17, 1943. Since the onset of the pregnancy she had experienced some loss of appetite, headache and periods of weakness. For several weeks before admission she had rather frequent attacks of what she thought were insulin reactions—palpitation, sweating, shortness of breath and a choking sensation.

Physical examination showed the following positive findings: diffuse but slight enlargement of the entire thyroid gland; slight accentuation of the basal heart sounds, especially on the aortic side; blood pressure 118 systolic, 82 diastolic; pulse rate 120 to 130; seven months' pregnancy. She was on the whole cheerful, but there appeared to be quite violent mood swings, when she became quite depressed.

Course.—Shortly after admission she began to have attacks of "insulin reactions"; blood sugar determinations made during these attacks were always elevated, and orange juice failed to relieve them quickly. These "spells" were always associated with tachycardia, and during one attack her pulse rate rose to 180. Two electrocardiograms taken two and five days after admission showed a normal sinus rhythm with a rate of 116 and 138 respectively, negative T_3 and a tendency to right axis deviation. It then came to our attention, from the Social Service Department, that her husband, who had been in the armed forces, was missing several months. It seemed probable that these alleged "insulin reactions" were, in all probability, anxiety attacks. She was seen in consultation by Dr. Mabel Ross from the Psychiatric Department, who concurred in the nature of the attacks. However, Dr. Ross believed that the patient's failure to accept the diabetes and her inability to live as other people did was also a contributing factor. No further attacks occurred after their nature was carefully explained to the patient and she had been assured that she would get along all right. On October 15, one week after admission, slight pretibial edema was first noted. There was no essential change in the blood pressure. The urine continued to be free of albumin and abnormal elements in the sediment.

On November 1 she had her first attack of diarrhea. These attacks continued several times each week—often as many as eight watery evacuations daily. These disappeared with the other evidences of toxemia. Several stools showed no occult blood. Culture of the feces was negative for pathogenic enteric organisms.

On November 23 the first trace of albumin in the urine was reported. This persisted and reached a 2 plus reaction by December 8.

On November 4 her blood pressure, which had been measured twice daily, showed its first conspicuous rise: 144 systolic, 84 diastolic; it continued to be essentially in that zone save for an occasional normal or rare higher reading until the toxemia improved.

On admission her red blood cells numbered 4,100,000, with 13.5 Gm. of hemoglobin per hundred cubic centimeters of blood. The white cells numbered 11,000, with 8 per cent bands, 56 filaments, 2 eosinophils, 30 lymphocytes and 4 monocytes. A slight anemia was first noted on November 18, when the red cells dropped to 3,500,000, with 9 Gm. of hemoglobin per hundred cubic centimeters. The leukocytes dropped to 7,900 per cubic millimeter, with no essential change in the differential. On November 26 the red blood cells numbered 3,660,000, with 11 Gm. of hemoglobin.

Two of our enterprising and interested clinical clerks, Mr. Melvin N. Wood and Mr. Paul J. Wolfgruber, determined the serum chorionic gonadotropic hormones on November 11. They were found to be at least 500 rat units per hundred cubic centimeters of blood. This was repeated again on November 26. Then one rat, which had a dose of serum corresponding to 1,700 rat units per hundred cubic centimeters, showed a corpus luteum, but the other rat, which received an amount corresponding to 1,000 rat units per hundred cubic centimeters of blood, showed no corpora lutea macroscopically. Just before her delivery an attempt was made to estimate the blood serum chorionic gonadotropic hormones. Unfortunately this was indeterminate.

On December 1 the patient was given diethylstilbestrol 2 mg. three times a day in the hope that it would alleviate the toxemia. Her weight, which had steadily increased from 58 Kg. (127½ pounds) on admission, had by this time reached 67 Kg. (147½ pounds). Coincident with the use of the diethylstilbestrol there was a prompt and gradual loss of weight with conspicuous diuresis, so that the weight was reduced to 62 Kg. (137 pounds) by the time of delivery on December 17. Also the systolic blood pressures were definitely lower, but the diastolic remained in the neighborhood of 90.

From the beginning the diabetes was difficult to manage. Except for the first two weeks, when the carbohydrate content in her diet was changed back and forth several times from 180 Gm. of carbohydrate to 140 Gm., her diet remained constant all through the observations at 160 Gm. of carbohydrate, 80 Gm. of protein and 110 Gm. of fat. A combination of protamine zinc insulin 90 units and unmodified insulin 30 units resulted in continuous glycosuria up to as high as 50 Gm. daily. An equal number of units of the unmodified insulin given in three doses—morning, evening and midnight—gave somewhat better control, but as the toxemia became more apparent this had to be increased gradually until the patient was receiving 90 units before breakfast, 68 before supper and 68 at midnight by December 1, when the diethylstilbestrol was started. The fast-

From the Buffalo General Hospital and the University of Buffalo School of Medicine.

1. White, P., and Hunt, H.: Pregnancy Complicating Diabetes: A Report of Clinical Results, J. Clin. Endocrinol. **3**: 500 (Sept.) 1943.

ing blood sugar on November 29 was 250 mg. per hundred cubic centimeters. Promptly after the administration of diethylstilbestrol, hypoglycemic reactions, which had not been present before, followed—fifteen in eleven days; in three of these, concentrated dextrose solution had to be given intravenously. This occurred in spite of the sharp reduction of the insulin dosage. The reactions did not cease until the dose had been lowered to 44 units in the morning, 30 units before supper and 10 units at midnight. It is interesting that there were but a few grams of dextrose in the urine even after the administration of 50 cc. of 50 per cent dextrose intravenously.

She was delivered on December 17 by Dr. Clyde Randall. Both her labor and her delivery were uneventful. She had an episiotomy. Caudal and chloroform anesthesia were used. Her blood pressure taken during labor was 120 systolic, 80 diastolic on one occasion and 128 systolic, 90 diastolic on another. The weight of the male fetus was 7 pounds 7 ounces (3,570 Gm.).

She required only slightly less insulin after delivery than she had previously: 36 units before breakfast, 16 before supper and 10 units at midnight.

She was discharged on a regimen of 180 Gm. of carbohydrate, 90 Gm. of protein and 120 Gm. of fat with 90 units of protamine zinc insulin and 16 of the unmodified insulin before breakfast. There was slight glycosuria occasionally during the day. Her fasting blood sugar was 182 mg. per hundred cubic centimeters. She had no insulin reactions.

SUMMARY

A primipara who was severely diabetic and who had had diabetes for twelve years was studied in the hospital for a period of three months.

The development of mild toxemia of pregnancy was observed—edema, albuminuria, diarrhea, mild hypertension and anemia. During this period the insulin requirement was nearly doubled. The chorionic gonadotropic hormones exceeded 500 rat units per hundred cubic centimeters of blood.

Soon after the oral administration of diethylstilbestrol 6 mg. daily the symptoms and signs of the toxemia disappeared, and the insulin dosage had to be promptly reduced because of the occurrence of many insulin reactions. At that time an estimation of the chorionic gonadotropic hormone was, unfortunately, indeterminate.

100 High Street.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following reports.

HOWARD A. CARTER, Secretary.

KREISELMAN RESUSCITATOR BELLOWS TYPE, MODEL 110, ACCEPTABLE

Manufacturer: The Ohio Chemical & Manufacturing Co., 1177 Marquette Street, Cleveland.

The Kreiselman resuscitator is designed to administer artificial respiration to all except the newborn. In general the apparatus as marketed consists of a bellows having an air and oxygen intake valves, an exhaust and a relief valve, a handle, an elbow connector for the face mask, an airway and a carrying case.

OPERATION

Administration of the air or air-oxygen mixture is accomplished by applying the mask over the patient's nose and mouth in airtight fashion and manually expanding and compressing the bellows. With the patient in the prone position, the head is turned slightly resting on the patient's hand as when using the prone pressure method of manual artificial respiration. When the patient is in the prone position the resuscitator is used with an elbow interposed between the exhaust valve of the bellows and the mask.

The oxygen intake valve has an inlet nipple to which a supply tubing for oxygen is attached. The valve is large enough to admit sufficient oxygen under pressure for therapeutic purposes. When the resuscitator is used with air only, this valve remains closed. The relief valve on the bellows operates at an internal pressure of 14 to 15 mm. of mercury and discharges freely the contents of the bellows at a pressure of 25 mm. of mercury.

The technic of operation is as follows:

1. Clear the mouth and throat of mucus and remove any foreign bodies from the mouth. Use a clean handkerchief or cloth if an aspirator is not available.
2. Place patient on back with hand extended, then carefully insert tip of airway above tongue along roof of mouth until the airway is well behind tongue thus holding it forward.
3. Keep chin raised.
4. Place mask over nose and mouth and hold it on airtight with one hand.
5. Operate bellows with other hand as follows:
   (*a*) Place the hand palm down under strap handle and raise bellows until filled with air.
   (*b*) Press down to compress the bellows until chest wall rises.
   (*c*) Release pressure at once by raising (expanding) the bellows.
   (*d*) Repeat this procedure of expanding and compressing the bellows at the rate of 18 times per minute.
   (*e*) When the patient makes breathing efforts, compress the bellows as he breathes in.
6. When resuscitation is attempted with the patient on his side or abdomen, turn the head to the side and use the bellows with the mask-elbow.
7. To use oxygen, attach supply tube to inlet valve on the bellows.

INVESTIGATIONS

One physician having had experience with this device reported that it was tested on a number of dogs that were asphyxiated. Controlled experiments were run using other kinds of mechanical apparatus for production of artificial respiration and also manually controlled appliances which are attached to anesthetic apparatus. The Kreiselman bellows type resuscitator was found to be as efficient as any of the other apparatus tried. The same physician said that the bellows resuscitator had been used successfully on 12 patients, all of whom had experienced respiratory arrest by inhalation of anesthetic agents. He reported that (1) asphyxia was not present in any of these cases, (2) all of the 12 patients were successfully and efficiently revived with the bellows type apparatus, (3) none of the patients died, (4) respiratory arrest in these patients was produced by an overdose of an anesthetic agent for the expressed purpose of testing the apparatus and (5) no impairment to the patient's lungs was noted either immediately or later.

Bellows resuscitator.

The Kreiselman (bellows type) apparatus together with the evidence submitted with it by this firm was referred to the Council investigator for examination and report. He stated that the device was used over a considerable length of time on patients purposely prepared for trial by stopping their respiration. The apparatus does what it is expected to do; namely, inflates the lungs with either air or oxygen under moderate positive pressure. The maximum pressure is controlled by a safety valve and is set to open long before dangerous pressures are reached.

The manufacturer expressed a desire to supply this apparatus to police and fire departments and other lay organizations that perform emergency artificial respiration on victims of drowning, gas poisoning, electric shock and so on. The firm was asked to submit reports of cases of asphyxia in which the device has been used successfully by lay operators in emergency cases. The firm replied that it was collecting these data but to date did not have enough records to satisfy the Council requirements.

The Council on Physical Medicine voted to accept the Kreiselman resuscitator for use in operating rooms and in medical institutions under the direction of a physician but voted not to accept it for use by lay organizations, because evidence is not available that a layman has successfully resuscitated an asphyxiated person with it.

THE FISCHER CRYSTAL SHORT WAVE DIATHERMY APPARATUS, MODEL VC, ACCEPTABLE

Manufacturer: The H. G. Fischer Company, 2323-2345 Wabansia Avenue, Chicago 47.

This apparatus applies heat to the tissues of the body for the treatment of disease. Where heat is indicated as a therapeutic measure, this appliance may be used. So far as it is known the immediate and only effect of medical diathermy is the production of heat, and the physiologic effects are those which normally follow the production of heat in the living tissues. This medical diathermy apparatus is built to meet not only the requirements of the Council on Physical Medicine but the requirements of the Army Medical Corps as laid down in the Federal Standard Stock Catalogue, section IV, part 5.

Model VC is a so-called crystal controlled apparatus. The frequency, 13,660 kilocycles per second (21.95 meter wavelength), does not, according to reliable evidence, vary from the norm more than 0.05 per cent; in fact, the tolerance of frequency stability is much less, and this under wide temperature and humidity variations.

The generator consists of a steel cabinet with an enamel finish, a steel chassis which may be removed and a control panel mounted to the chassis with all controls thereon. The chassis consists of three units; namely a crystal control, a buffer and a final amplifier. The crystal control and buffer compartment may be removed from the chassis for repair or replacement by removing a screw at the base clamp of the buffer compartment. When the crystal is removed, the entire generator is disconnected from the power supply. An overload switch is also provided to protect the unit against short circuits. Connections for treatment electrodes are provided at the side of the unit. Treatment is applied by means of a cable or drum. It weighs approximately 200 pounds.

Fischer Crystal Short-wave Diathermy.

The ability of the apparatus to heat tissue was tested in a laboratory acceptable to the Council. The report is as follows:

The method followed was: 3 turns of cable around thigh, overall measurements 7 to 8 inches, one hand towel and ⅜ inch layer of felt between cable and skin. Skin hyperemia was observed.

TABLE 1.—*Cable Technic*

Experiment Number	Deep Muscle Initial	Temperature of Final	Oral Temperature, F. Initial	Oral Temperature, F. Final
1	97.1	106.5	98.3	99.0
2	97.4	106.2	98.3	99.2
3	97.4	107.0	98.3	99.5
4	97.5	104.9	98.6	99.7
5	97.6	104.7	98.8	99.8
6	97.6	105.4	99.0	100.0
Average	97.4	105.8	98.5	99.5

TABLE 2.—*Disk Technic*

Experiment Number	Deep Muscle Initial	Temperature of Final	Oral Temperature, F. Initial	Oral Temperature, F. Final
1	97.0	104.2	98.5	98.4
2	97.6	104.3	98.4	98.7
3	97.3	104.0	98.5	98.8
4	97.7	105.5	98.8	99.1
5	97.8	105.5	98.8	99.4
6	97.8	105.0	98.9	99.5
Average	97.5	104.9	98.6	99.0

The method followed for the disk technic was: 10½ inch diameter disk applied obliquely to the thigh with one layer of toweling between surface of disk and the skin, center of disk opposite center of cannula. Blebs were produced as the result of point heating.

Heating-load test reveals that the transformers meet the requirements of the Council. The report from a laboratory recognized by the Council as qualified to judge on the frequency stability indicates that the crystal control feature maintains a stability within 0.05 per cent.

The apparatus operates on 115 volts alternating 60 cycle current. The lamp load test shows an output of 200 watts. On practical test the apparatus proved to stand up well when used clinically.

The Council on Physical Medicine voted to accept the Fischer Crystal Short Wave Diathermy apparatus, Model VC, for inclusion in its list of accepted devices.

Council on Foods and Nutrition

The following report, authorized by the Council for publication, represents the completion of the study of the nutritive value of prepared cereal foods made under a grant of the Board of Trustees at the request of the Council.

GEORGE K. ANDERSON, M.D., Secretary.

VITAMIN CONTENT OF PREPARED CEREAL FOODS

GEORGE KITZES, PH.D.
AND
C. A. ELVEHJEM, PH.D.
MADISON, WIS.

A preliminary report on the thiamine, riboflavin and niacin content of a number of prepared cereal products was published in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Dec. 4, 1943. More extensive data are tabulated in the accompanying table. Some new products have been included, but the main purpose of the additional work was to determine the variation in the vitamin content of the typical products on the market. The cereals were purchased from grocery stores in different parts of Madison and from stores having a rapid turnover in order to avoid products kept on the shelves for long periods of time. Most of the samples were obtained at three different periods, spring, summer and fall of 1943. The thiamine was determined by the thiochrome method [1] and the riboflavin and niacin by microbiologic procedures.[2]

The values for whole grains are included again for comparison. The products to which restorative additions of synthetic vitamins or vitamin concentrates have been made are indicated with an asterisk. Others enriched according to proposed federal standards of enrichment are appropriately indicated. When the individual samples gave values within rather narrow limits, one average figure is given; when a greater variation was observed, the range of figures is included.

The variation between samples of the same product purchased at different periods is surprisingly small. The restored and enriched products gave the most variable results, owing undoubtedly to the higher vitamin content and to difficulties in obtaining uniform distribution of the added vitamins. Some of the products low in thiamine also showed considerable variation, probably because of differences in the degree of processing.

It is interesting to note that a large percentage of the wheat products and practically all of the corn, oats and rice products contain levels of thiamine within the range for the whole grains. Very few of the riboflavin values fall below the corresponding minimum whole

From the Department of Biochemistry, College of Agriculture, University of Wisconsin.

Published with the approval of the director of the Wisconsin Agricultural Experiment Station.

1. Hennessy, D.: The Determination of Thiamine in Cereal Products, Cereal Chemist Bull. **2**, 1942.

2. Strong, F. M., and Carpenter, L. E.: Preparation of Samples for the Microbiological Determinations of Riboflavin, Indust. & Engin. Chem. (Anal.) **14**: 909, 1942. Krehl, W. A.; Strong, F. M., and Elvehjem, C. A.: Determination of Nicotinic Acid, ibid. **15**: 471, 1943.

grain values. The biggest discrepancy occurs in the niacin values for wheat. Very few of the products, even when the vitamin has been added, meet the minimum values of 5.4 mg. for 100 Gm. The reason for this is readily evident. Wheat bran is very rich in niacin, and the bran is generally removed in the preparation of the wheat products. Further consideration may have to be given this standard, but in any case a product designated as containing added niacin should contain more than 4 mg. per hundred grams.

In summary it is evident that the cereal manufacturers have made excellent progress in improving and standardizing their products. Sufficient data are now available to allow rather accurate estimation of the amount of thiamine, riboflavin and niacin contributed by most of the commercial products.

In the process of handling the numerous brands of prepared cereal foods which were examined, the lack of uniformity in the expression of nutritional values on the package was quite apparent. Some are expressed in terms of the average serving, others as a 1 ounce serving or on a pound basis, giving the percentage of the minimum daily requirements in some cases and in others the milligrams or international units contained therein. It is difficult or impossible for the average person to make an intelligent comparison of the nutritional content of the various cereal products by examining the labels. On the other hand, if these values could be expressed on the uniform basis of the average 1 ounce serving with the nutritional content in terms of percentage of daily requirements as well as actual milligrams (or international units for vitamins A and D) supplied, a better understanding and appreciation by the housewife and nutritionist of the food value of the various types of cereal products would be realized.

Vitamin Content of Whole Grains

A majority of samples of whole grains contain the indicated nutrients in amounts within the following ranges
(Data Compiled by the Food and Nutrition Board, National Research Council)

Product	Thiamine	Riboflavin	Niacin
	(Expressed as Mg. per 100 Gm.)		
Wheat, whole	0.44 to 0.66	0.09 to 0.20	5.4 to 8.0
Corn, whole	0.37 to 0.58	0.08 to 0.24	1.7 to 2.7
Oats	0.66 to 0.88	0.12 to 0.17	0.88 to 1.8
Rice	0.33 to 0.56	0.08 to 0.25	4.4 to 6.6

Vitamin Content of Prepared Cereal Foods

	Manufacturer			
Products Derived from Wheat				
All-Bran	Kellogg Company	0.37 to 0.52	0.36 to 0.48	16.0 to 18.5
Post's Bran Flakes *	General Foods Corporation	0.45 to 0.55*	0.21 to 0.29	7.5 to 9.0
Chef White Wheat Cereal	IOA Foods	0.06	0.06	1.0
Coco-Wheats *	Little Crow Milling Company	0.39 to 0.48*	0.07	1.9 to 2.3*
Cracked Wheat	Doughboy Mills, Inc.	0.44	0.16	4.4
Cracked Wheat	IOA Foods	0.40	0.17	4.5
Cream of Wheat **	Cream of Wheat Corporation	0.41 to 0.68*	0.06 to 0.10	1.6 to 2.0*
Farina **	Pillsbury Flour Company	0.40*	0.05	2.0*
Force	The Best Foods, Inc.	0.04	0.16	4.1
Grape-Nut Flakes *	Post Products	0.52*	0.17 to 0.26	4.9 to 5.6
Grape-Nuts Wheat Meal *	Post Products	1.02*	0.12	5.1
Grape-Nuts *	Post Products	0.81*	0.17 to 0.20	3.9 to 4.9
Hecker's Cream of Farina **	The Best Foods, Inc.	0.40*	0.06	2.4*
Krumbles	Kellogg Company	0.02 to 0.07	0.16 to 0.21	4.2
Maltex Cereal	Maltex Company	0.35	0.13 to 0.17	4.5
Malt-O-Meal *	Campbell Cereal Company	0.40 to 0.60*	0.25 to 0.32*	2.7 to 3.3*
Pep *	Kellogg Company	1.2 to 1.5*	0.16 to 0.25	4.5 to 6.5
Puffed Wheat Sparkies *	Quaker Oats Company	0.40 to 0.54*	0.12 to 0.16	8.4*
Ralston Whole Wheat Cereal †	Ralston Purina Company	0.53	0.14	4.0 to 5.1
Rolled Wheat	Doughboy Mills, Inc.	0.37	0.13	4.1
Rolled Wheat	IOA Foods	0.32	0.14	4.0
Rolled Wheat (Pettijohn's)	Quaker Oats Company	0.31 to 0.40	0.13 to 0.16	3.8
Shredded Ralston	Ralston Purina Company	0.11 to 0.16	0.13	4.3
Shredded Wheat	Kellogg Company	0.19 to 0.23	0.14 to 0.19	4.5
Shredded Wheat	National Biscuit Company	0.24	0.13 to 0.15	4.2
Shreddies	National Biscuit Company	0.20	0.12	4.0
Wheatena	Wheatena Company	0.06 to 0.13	0.15	4.0
Wheaties *	General Mills Company	0.39 to 0.60*	0.19 to 0.22*	4.1 to 5.1
Wheatsworth	National Biscuit Company	0.50	0.13	4.8
Products Derived from Corn				
Corn Flakes *	Kellogg Company	0.39 to 0.45*	0.08	1.6*
Corn Flakes *	Post Products	0.28 to 0.40*	0.10	1.3
Kix *	General Mills Company	0.44 to 0.59*	0.10 to 0.20	2.1 to 2.7*
Products Derived from Oats				
Cheerioats *	General Mills Company	0.84*	0.25*	2.0*
H-O Quick Oats	The Best Foods, Inc.	0.67	0.17	0.85
Mother's Oats	Quaker Oats Company	0.61	0.17	0.85
Quaker Oaties *	Quaker Oats Company	0.63 to 0.90*	0.11 to 0.15	0.60 to 0.7
Quick Quaker Oats	Quaker Oats Company	0.58 to 0.70	0.14 to 0.18	0.83 to 1.0
Products Derived from Rice				
Cream of Rice	Grocery Products Mfg. Company	0.16	0.08	1.7
Cream of Rice *	Grocery Stores Product Sales Co., Inc.	0.94*	0.62*	6.3*
Puffed Rice Sparkles * (new)	Quaker Oats Company	0.64*	0.06	4.6*
Rice Krispies *	Kellogg Company	0.45*	0.07	8.0*
Rice—Natural Brown	Comet Rice Mills	0.41	0.09	4.4
Products Not Otherwise Classified				
Cerevim * †	Lederle Laboratories	2.1*	3.3*	20.3*
Cream of Rye	Fruen Milling Company	0.12	0.17	0.92
Life of Wheat-Wheat Germ	Life of Wheat Company	2.3	1.0	4.5
Scotch Brand Barley (Pearled)	Quaker Oats Company	0.15	0.07	2.1
Soya Wheat	Soya Wheat Company	0.71	0.27	3.4
Viobin Wheat Germ	Viobin Corporation	3.0	1.2	5.5

* Restorative addition of synthetic vitamin or vitamin concentrate.
** Enriched with synthetic vitamins or vitamin concentrates to conform with proposed federal standards of enrichment.
† Added wheat germ.

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SATURDAY, SEPTEMBER 9, 1944

THE CHICAGO VIVISECTION FUROR

For some weeks Chicago has been treated to a spectacle such as only Chicago can furnish, because the self-elected star of the performance is Irene Castle, once noted as half of a terpsichorean team and now maintaining a somewhat aging reputation by periodic appearances in the limelight in behalf of a dog shelter called Orphans of the Storm and in behalf of a general attack against all experiments with animals. Listed in the supporting cast is Mr. William Randolph Hearst of California and New York, who places the Chicago *Herald American* and all its staff at Miss Castle's disposal during the run of the play. Fortunately for the American people and fortunately also for the scientific medical institutions of Chicago, every other newspaper in the city has recognized the menace of the Castle-Hearst combination and has come to the support of the Chicago leaders of medical education with the amount of space and the vigor demanded by the antivivisectionist shrieking. The pity of it all is that so much important space and time should have to be devoted in the war effort to meeting this stupid and obsolete sentimentalism.

The City Council of Chicago a good many years ago passed an ordinance that makes available the use of stray dogs for scientific medical study. Apparently some of the aldermen have been high pressured by Mr. Hearst's campaign into introducing an amendment to the city code which would make it difficult or impossible for medical science to get the necessary number of dogs to carry on. Specifically, it proposes to repeal the ordinance under which stray dogs in the city pound go to medical schools because their owners fail to reclaim them after five days.

The campaign of the *Herald American* featured what was said to be the eye witness story of a former employee of the medical school of the University of Chicago. This man had served as an animal caretaker for only six weeks and left his position without notice just a few days before the first article appeared in the *Herald American.* Apparently he had used his time to take pictures surreptitiously—pictures which were harmless in themselves but which were made to appear brutal and improper by the captions printed under them. The evidence is positive that the laboratories in question utilize animals with the utmost discrimination, without subjecting them to unnecessary pain or discomfort, carrying out all operative experiments under anesthesia and in accordance with the same standard of procedure that is used in hospitals everywhere throughout the country. The attack was centered on Dr. Dallas B. Phemister, professor of surgery, whose character and reputation as a distinguished scientist need no defense. The fact that the attack would be centered on a surgeon of distinction for his scientific accomplishments and his devotion to the healing of disease is an indication of the stress to which the antivivisectionists were put in order to make any kind of case whatever. Opposed to the ridiculous presentation which the antivivisectionists made before the city council were the professors of physiology in all the medical schools, the statements of the Surgeons General of the Army, Navy and U. S. Public Health Service and the personal appearance of Major General George F. Lull, Deputy Surgeon General of the Army. The incident served to bring out the tremendous advancement that medical science has made in recent years, largely by the use of animal experimentation. Long since and repeatedly it has been emphasized that dogs themselves have benefited, as well as has man, by the very experimentation that this illogical group condemns.

The Journal of the American Medical Association wishes to commend the medical scientists of Chicago for having given so much of their time and their energy to meeting this challenge. The preparation which they made for the hearings before the city council, with the attendance of all the medical students of the city in uniform at the sessions, the orderly and painstaking presentation of the case, may well be models for similar efforts when a similar challenge happens to arise elsewhere in the nation or even in Washington. Yet it all comes down to a paragraph from a statement in an editorial in the Chicago *Tribune,* which gave many columns to interviews and editorials during the weeks preceding the hearing.

The *Tribune* said:

> There comes a time when patience with people like this ceases to be a virtue. It is no excuse to plead for them that they are sincere. So, probably, is Hitler, who is no crazier than some antivivisectionists.

STREPTOTHRICIN

In 1941 Waksman of the New Jersey Agricultural Experiment Station isolated a bactericidal substance from a soil streptothrix (Actinomyces lavendulae), which he named "streptothricin."[1] Streptothricin is completely adsorbed on charcoal from a fluid culture medium from which it can be recovered by treatment with dilute acid. Waksman found that the crude product thus prepared had a definite inhibitory action on the majority of the bacterial species he tested. As little as 0.1 mg. of the product added to 10 cc. of nutrient agar completely prevented the growth of Escherichia coli and many other gram negative bacteria. Gram positive bacteria were of variable resistance, some being extremely sensitive to this bacteriostatic agent while others were highly refractory. Streptothricin also had a decisive antibiotic action against numerous fungi and yeasts.[2]

A preliminary report on the therapeutic efficiency of this bacteriolysin has been made by Robinson and his associates[3] of the Merck Institute for Therapeutic Research, Rahway, N. J. The crude streptothricins tested by these investigators varied in potency from 5 to 300 units per milligram, the unit being the minimum quantity of the crude product which added to 1 cc. of nutrient broth completely inhibits the growth of a selected strain of E. coli. The toxicity of these products was tested by administering a single dose intravenously, subcutaneously or by mouth to each of a selected group of 10 mice. Mice given as much as 30,000 units per kilogram of body weight intravenously, 60,000 units subcutaneously or 250,000 units orally showed no evidence of toxicity. When twice these doses were administered, anorexia accompanied by a gradual loss of weight was noted in most of the mice, with a 20 per cent mortality.

Confirming Waksman's data, the bacteriostatic titers were determined by incorporating various amounts of each product in melted blood agar and streaking the surface of the solidified agar with a variety of pathogens. The minimum amount of streptothricin necessary for bacteriostasis varied with different bacterial species. Eberthella typhi was completely inhibited by as little as 4 units of streptothricin per cubic centimeter, while Escherichia coli, Staphylococcus aureus, Salmonella schottmülleri, Diplococcus pneumoniae, Bacterium flexneri and certain strains of Streptococcus haemolyticus required from 16 to 32 units. Streptococcus viridans and Streptococcus lactis were refractory, 1,024 units giving only partial growth inhibition. Intermediary groups included several strains of Streptococcus haemolyticus, Staphylococcus aureus, Neisseria meningitidis, Proteus vulgaris and Aerobacter aerogenes.

Therapeutic tests were made on groups of 30 to 60 mice. Each mouse was inoculated intraperitoneally with 10,000 lethal doses of a selected pathogen. Treatment was begun immediately after inoculation. The therapy consisted of either a single or a repeated dose of streptothricin given intravenously, subcutaneously or by mouth. A single dose of 50 to 100 units (a tenth of the toxic dose) given subcutaneously shortly after inoculation apparently affords complete protection against Salmonella schottmülleri, Escherichia coli and Bacterium shigae, while 3,000 units was required for the same therapeutic effect if the drug was given by mouth. With relatively refractory micro-organisms, such as Pseudomonas aeruginosa, Staphylococcus aureus and Diplococcus pneumoniae, practically no beneficial effects were noted, even when the dose was increased tenfold, i. e. approaching the toxic range. It was also noted that streptothricin given by mouth reduces the normal lactose fermenting flora of the gastrointestinal tract.

Robinson suggests that in time streptothricin may prove to be of value in the treatment of bacillary dysentery, typhoid and colon infections. If so, it would function as a valuable supplement to penicillin, which has little or no therapeutic action against these gram negative infections.

1. Waksman, S. A., and Woodruff, H. B.: Proc. Soc. Exper. Biol. & Med. **49**: 207, 1942.
2. Foster, J. W., and Woodruff, H. B.: Arch. Biochem. **3**: 241, 1943.
3. Robinson, H. J.; Graessle, O. E., and Smith, D. G.: Science **99**: 510 (June 30) 1944.

ABORTIVE OR NONPARALYTIC POLIOMYELITIS

Fortunately the most frequent clinical form of poliomyelitis is the abortive or nonparalytic. Similar transitory infections may occur in the experimental disease in monkeys. In both cases the absence of paralysis is not necessarily due to failure of the virus to invade and multiply in the tissues of the central nervous system but to limitation of its spread therein. The limitation may depend on the virus, on the host or on both. Faber, Silverberg and Dong[1] studied the resistance to a strain of virus of the cynomolgus monkey under well controlled experimental conditions. They found that nontraumatic exposures to the virus of the respiratory and alimentary mucous membranes of cynomolgus monkeys may be followed by a definite resistance to later intracerebral inoculations of the virus. In such cases typical lesions were found in the central nervous system descending from the level of the inoculation into the brain stem and to a much more limited extent into the cord. There were no indications of any invasion of the central nervous system previous to the intracerebral inoculation, but lesions were found in the peripheral ganglions corresponding to the mucous membranes previously exposed to the virus.

1. Faber, H. K.; Silverberg, R. J., and Dong, L.: Poliomyelitis in the Cynomolgous Monkey: II. Resistance to Spread of Infection in the Central Nervous System Following Exposures of Mucous Membranes to Virus, with Comments on Nonparalytic Poliomyelitis, J. Exper. Med. **78**: 519 (Dec.) 1943.

This limitation of spread of experimental poliomyelitis in monkeys resembles the stop in the evolution of human poliomyelitis which results in the clinical gradations represented by abortive, nonparalytic and mildly paralytic forms of the disease. It may be assumed that natural exposures to the virus lead to increase in the resistance to its invasion of the central nervous system, possibly due to the development of specific antibodies. Whether natural human exposures to the virus which do not result in clinical poliomyelitis may leave lesions in peripheral ganglions, as was the case in the experiments on monkeys, is a question. Postmortem study of these ganglions, especially in children, with this question in mind might well be worth while.

At present there seems to be no practical way of increasing successfully the resistance to human poliomyelitis by artificial means. Previous efforts to that end led to the conclusion that the injection of killed virus is not effective. A safe method of immunizing with modified living virus has not yet been found.

AIR BORNE POLIOMYELITIS

The epidemiology of human poliomyelitis has recently directed attention largely to the presence of the virus in feces and sewage and to the growing conviction that infection with poliomyelitis virus is usually by way of the alimentary tract. The demonstration by Faber and his associates [1] of Stanford University of the ease with which the upper portions of the alimentary tract of monkeys can be penetrated by the virus has intensified this concept. A modification of this belief will presumably follow recent studies of the virus content of nasopharyngeal secretions of clinical cases and attempts to infect experimental animals with air borne virus. Up to five years ago, out of 287 clinical trials the virus of poliomyelitis had been isolated but 29 times from the human nasopharynx.[2] Paul [3] concluded from such data that less than 6 per cent of the poliomyelitis patients had viable virus on the nasopharyngeal surfaces, an insignificant percentage when compared with the great frequency with which the same virus is present in the stools or colonic washings in clinical cases.

A different perspective is suggested by a resurvey currently reported by Howe and his associates [4] of Johns Hopkins University. Howe discarded the nasopharyngeal irrigation technic of earlier investigators and obtained secretions from the posterior wall of the oropharyngeal surface and the peritonsillar areas by means of cotton swabs. The two swabs used with each patient were detached, dropped into 1 cc. of sterile water and stored on solidified carbon dioxide. The two swabs were afterward eluted in phosphate buffer solution and the fluid pressed out or sucked out by a syringe. The resulting fluid was rendered bacteriologically sterile by a thirty-six hour contact with a quarter volume of ether, after which the ether was removed. The yield was usually 1.1 cc. of fluid from each patient. The entire specimen was inoculated intracerebrally into a rhesus monkey, half of the sample being injected into each lateral thalamus. This region was chosen because of its relatively high susceptibility to the virus and because its deep position minimized the danger of leakage or backflow.

Specimens have been tested from 14 random cases of juvenile poliomyelitis, all tests being made during the first week of the disease. Of this group 7 specimens produced typical and usually lethal poliomyelitis in rhesus monkeys, the positive results being equally distributed between paralytic and nonparalytic human cases. If fully confirmed, this high percentage would suggest that nasopharyngeal secretions play a much more important role in the spread of poliomyelitis virus than had been previously concluded. Many human cases would presumably be due to air borne droplet or dust infection.

This suggestion is made highly plausible by studies of the infectivity of air borne poliomyelitis virus, currently reported by Faber and his associates [5] of Stanford University. The Stanford experimenters used an improved atomizing flask into which a virus suspension can be delivered as a fine spray. All unevaporated droplets are retained in the flask and an even suspension of dry droplets or "droplet nuclei" passed into a large respiratory chamber. This chamber accommodates the heads of 4 monkeys under anesthesia with pentobarbital sodium. After one hour exposure to the virus infected air 5 of the 7 rhesus and 6 of the 7 cynomolgus monkeys thus far tested developed typical poliomyelitis. Histologic evidence indicated that the virus had entered the central nervous systems of all 11 monkeys through the olfactory nerves. To study other possible respiratory ports of entry the test was repeated on 35 rhesus and 10 cynomolgus monkeys in which olfactory blockade had been induced by previous application of 1 per cent zinc sulfate. Of these, 2 rhesus monkeys and 4 cynomolgus monkeys developed typical poliomyelitis. Serial sections indicated that the nonolfactory port of entry was in most cases through the afferent fibers of the fifth cranial nerve, entrance by way of the local sympathetic fibers being demonstrated in but 1 case.

Faber concludes from these tests that the concept of poliomyelitis as an air borne disease acquired by inha-

1. Faber, H. K.; Silverberg, R. J., and Dong, L.: J. Exper. Med. **78**: 499 (Dec.) 1943.
2. Vignec, A. J.; Paul, J. R., and Trask, J. D.: Yale J. Biol. & Med. **11**: 15 (Oct.) 1938.
3. Paul, J. R.: Infantile Paralysis, a symposium delivered at Vanderbilt University, Waverley Press, Lecture 5, p. 127, 1941.
4. Howe, A. A.; Wenner, H. A.; Bodian, D., and Maxcy, K. F.: Proc. Soc. Exper. Biol. & Med. **56**: 171 (June) 1944.
5. Faber, H. K.; Silverberg, R. J., and Dong, L.: J. Exper. Med. **80**: 39 (July) 1944.

lation of contaminated air or dust deserves more consideration. Such a view, he emphasizes, does not exclude ingestive infection, since experiments have shown that in monkeys infection occurs with equal ease by the two ways. Which mode of infection is the more important for man is a problem that still awaits solution.

MALNUTRITIONAL ANTIVIRAL IMMUNITY

Reasoning from experimental evidence obtained from a study of bacterial infections, many clinicians have assumed that resistance to pathogenic viruses would be lowered as a result of dietary deficiency and that prophylactic effects would follow the administration of corrective doses of such factors as ascorbic acid, thiamine, riboflavin, nicotinic acid and pantothenic acid. This line of reasoning was challenged in 1939 by Foster and his associates [1] of the department of pediatrics, University of Pennsylvania School of Medicine, who studied the effects of thiamine deficiency on resistance to poliomyelitis virus.

Litters of white mice varying from 21 to 31 days of age were split into two groups. One group was fed ad libitum a standard diet containing 100 micrograms of thiamine per hundred grams. The second group was placed on a similar diet in which the thiamine content had been reduced to 10 micrograms per hundred grams. Fifteen to twenty days later each mouse was injected intracerebrally with 0.03 cc. of a 0.5 per cent suspension of virus infected mouse brain (Lansing strain), control injections being made with 0.5 per cent suspension of normal mouse brain. Typical paralysis was noted in 74 per cent of the mice at the optimum thiamine level, as contrasted with but 13 per cent paralysis in the thiamine deficient group.

With a third group of mice the thiamine content of the ingested food was raised to 30 micrograms per hundred grams (minimum maintenance level). In this group 17 per cent of the injected mice developed paralysis. The conclusion was drawn that even a partial reduction in optimum thiamine intake increases resistance to poliomyelitis virus. Foster [2] subsequently found that mere restriction of caloric intake without reduction in ingested thiamine resulted in a similar though less definite increase in resistance to poliomyelitis.

These results were afterward confirmed by Rasmussen and his associates [3] of the University of Wisconsin, who tested four carefully selected mouse groups. The first group was fed a synthetic diet containing optimum amounts of all necessary food factors except thiamine. On this diet the mice developed an acute deficiency, characterized by rapid loss of weight. A second group of mice was fed the same diet plus a minimum maintenance amount of thiamine (30 micrograms per hundred grams), on which diet the weight remained constant for at least thirty days. A third group was fed the same diet plus an optimum amount of thiamine (200 micrograms per hundred grams). On this diet the weight increased rapidly. A fourth group was fed an excessive amount of thiamine (600 micrograms per hundred grams). Thirteen days after the animals had been placed on these diets each mouse was injected intracerebrally with 0.03 cc. of a 2 per cent brain-cord suspension of the Lansing mouse adapted poliomyelitis virus. Within fourteen days 81 per cent of the mice at the optimum or excessive thiamine level developed paralysis, while but 14.2 per cent of those on the thiamine free diet became paralyzed. Of those at the minimum maintenance level 50 per cent became paralyzed.

Rasmussen also tested a fifth group of mice in which there was a restricted caloric intake without a reduction in the thiamine or other vitamin factors. The control morbidity of 81 per cent was reduced to 65 per cent in this group. The Wisconsin bacteriologists then broadened their field of research to include tests with Theiler's encephalomyelitis virus injected intraperitoneally. Here the differences in resistance were of the same order but less pronounced than with poliomyelitis virus, the control morbidity of 55 per cent being reduced to 42 per cent as a result of thiamine deficiency. The field of research was then widened to include the effects of restricted intake of pantothenic acid.[4] They found that Swiss mice fed a synthetic ration deficient only in calcium pantothenate exhibited a definitely increased resistance to Theiler's encephalomyelitis virus. There was, however, little or no increased resistance to poliomyelitis virus.

A theory to account for this malnutritional antiviral immunity was suggested in 1942 by Sprunt [5] of Duke University, who studied the resistance of undernourished rabbits to intradermal injection with vaccinia virus. In all cases the resulting lesions were fewer and smaller in the malnutrition group than in adequately fed controls. Sprunt interpreted this as evidence that vaccinia virus is less able to multiply in poorly nourished tissue cells than in adequately nourished cells. With this theory a malnutritional hypersusceptibility to bacterial infections coupled with a partial malnutritional immunity to virus diseases ceases to be paradoxical.

Sprunt's theory is based on the classic assumption that the virus particle is a living parasite feeding on or in competition with the invaded tissue cell. A more complex theory would be necessary if the virus was pictured as a giant protein molecule multiplied by the engrafted cell.

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1. Foster, C.; Jones, J. H.; Henle, W., and Dorfman, F.: Proc. Soc. Exper. Biol. & Med. **51**: 215, 1942.
2. Foster, C.; Jones, J. H.; Henle, W., and Dorfman, F.: Science **97**: 207, 1943.
3. Rasmussen, A. F.; Waisman, H. A.; Elvehjem, C. A., and Clark, P. F.: J. Infect. Dis. **74**: 41 (Jan.-Feb.) 1944.
4. Lichstein, H. C.; Waisman, H. A.; Elvehjem, C. A., and Clark, P. F.: Proc. Soc. Exper. Biol. & Med. **56**: 3 (May) 1944.
5. Sprunt, D. H.: J. Exper. Med. **75**: 297, 1942.

Current Comment

POSTWAR TRAFFIC DANGERS

Automobile traffic hazards will no doubt begin to increase almost at once after the end of the war. Methods to control this problem should receive careful consideration now. The National Safety Council has just published an excellent brochure on postwar traffic problems for a group of forty sponsoring organizations, including the American Medical Association. According to this booklet the long-term problems will include greater traffic volumes and speeds, probable changes in traffic and parking patterns, new developments in automobile design, continued if not increased night traffic hazards, and no anticipated decrease in the accidents resulting from drinking alcoholic beverages. Safety measures devised and instituted, although unevenly, before the war must be continued and implemented. Especially important will be training of adequate personnel to meet the new and perhaps unexpected problems which will surely arise. New measures must be introduced to cope with new problems. Road construction, betterment of existing streets and highways, and traffic engineering administration will play a part in preventive measures. New technics will have to be devised for police personnel and their equipment; standard technics of enforcement can be more widely adopted. Vehicle inspection, driver licensing, traffic safety instruction and education are additional measures which will require careful application. About 35,000 deaths and well over a million injuries annually from automobile accidents were recorded during recent prewar years; all evidence indicates that this cause of death and injury will rise to new heights in the postwar period unless adequate preventive measures are taken.

BIOLOGIC SYNTHESIS

The older view, championed by Liebig, considered that the chemistry of the animal body was destructive in character, whereas in plants widespread synthesis took place. Subsequent investigation has shown the fallacy of this concept; there is ample evidence that fat and carbohydrate are synthesized from unlike precursors, while purines, hormones and aminoacetic acid, among other compounds, are known to be products of biochemical synthesis in the animal body. The most recent evidence on this general point relates to beta-alanine, a nitrogenous constituent of the muscle extractives carnosine and anserine. Although alpha-alanine is a common amino acid obtained from most proteins, the beta analogue has been considered a biochemical novelty. Interest in this compound was increased when it was discovered [1] that it constitutes part of pantothenic acid, one of the vitamins of the B group. It becomes of interest to know whether or not the growing animal can synthesize the beta-alanine in its tissues. Using weanling rats, Schenck and du Vigneaud [2] have shown that the beta-alanine in the nonhepatic tissues increases some twenty times in the fifty days after weaning and that this increase is independent of the amount of beta-alanine in the diet. As the tissue extractives assume greater importance in the metabolism of muscle —quantitatively the most important tissue in the body —the origin and availability of these compounds becomes of greater interest.

1. Williams, R. J., and Major, R. T.: Science **91**: 246, 1940.
2. Schenck, J. R., and du Vigneaud, V.: J. Biol. Chem. **153**: 511 (May) 1944.

THE HETEROLOGOUS TRANSPLANTATION OF HUMAN CANCERS

Greene and Lund [1] have reported successful transplantation of a series of 10 human cancers to the anterior chambers of eyes of guinea pigs. The series contained a fibrosarcoma of the chest wall, an adenocarcinoma of salivary gland tissue, a chondromyxosarcoma of the larynx, a malignant melanoma, an epidermoid carcinoma of the buccal mucosa, an adenocanthoma of the urethra, a mammary fibrosarcoma, an undifferentiated carcinoma of the lung, an epidermoid carcinoma of the lung and a chordoma. The transplants grow progressively in the alien host and bear a close microscopic resemblance to the original tumors. In the majority growth became apparent in all successful transplants within several days. In earlier experiments with rabbit tumors the authors failed to transplant benign tumors or tumors in their preinvasive stage. Apparently, therefore, heterotransplantability may be a characteristic property of cancer. More recent experiments demonstrate that in man as well as in rabbit cancer autonomy or transplantability transcends species barriers. Numerous attempts to transfer benign human tumors to lower animals have failed. Transplantation experiments utilizing biopsy tissue from precancerous lesions and from anaplastic tumors during preinvasive stages likewise failed. Transplantability of malignant tumors to lower animals, it is pointed out, may serve as a diagnostic aid in a case of questionable tissues and assist in the morphologic classification of cancers. Cancers may be associated with local tissue reaction that obscures the nature of the cell involved in the neoplastic process. Thus the tissue obtained from the first biopsy of the fibrosarcoma of the chest wall in 1 of their cases contained a large number of giant cell forms and the question of muscular origin arose. However, only the fibroblastic elements survived guinea pig transfer, and it became clear that the growth was fibrosarcoma and that the giant cells were reactive rather than neoplastic in nature. It is also pointed out that transplants often show a slightly higher degree of cellular differentiation and organization than is found in the primary host and thus allow a classification of highly anaplastic tumors. This was demonstrated in their case of transplanted chordoma. The ability to grow cancer in lower animals affords an approach to many other problems associated with human tumors. After successful primary transplantation the cancer can be carried by serial passage to new generations of animals and subjected to a variety of investigations not permissible in the human host. After preliminary growth in the anterior chamber of the eye, transfer to other body regions is readily effected.

1. Greene, Harry S. N., and Lund, Paul K.: The Heterologous Transplantation of Human Cancers, Cancer Research **4**: 352 (June) 1944.

MEDICINE AND THE WAR

ARMY

REORGANIZATION OF OFFICE OF SURGEON GENERAL

It has recently been announced from the office of the Surgeon General of the Army that the post of Assistant Surgeon General is to be filled by Brig. Gen. Raymond W. Bliss. The post is newly created as a part of a recent reorganization. General Bliss will hold the new post in addition to his duties as chief, Operations Service.

The Administrative Service is dissolved, as part of the reorganization: the Fiscal, Legal and Office Service Divisions will report directly to the executive officer as previously. In place of the Professional Service, four Professional Consultant Divisions are being created: medical, surgical, neuropsychiatric and reconditioning. All personnel of the Nursing Division, another division to be dissolved, and related aspects of the Army Nurse Corps will be the responsibility of the Army Nurse Branch of the Military Personnel Division, Personnel Service. The overall policy aspects of the Army Nurse Corps will be the responsibility of the newly constituted Nursing Division of the Professional Administrative Service.

A new Professional Administrative Service is being created, with Col. Arden Freer as chief and Col. Esmond R. Long deputy chief. The following will be included: Physical Standards Division, Nursing Division, Medical Statistics Divison, Professional Inquiries Unit, Women's Health and Welfare Unit. Col. Florence A. Blanchfield will be director of the Nursing Division, Professional Administrative Services.

SURGICAL OPERATING TRUCKS TAKE HOSPITAL TO WOUNDED SOLDIERS

The Army Medical Department has established mobile surgical groups which provide hospital facilities for wounded soldiers near the front lines. The tent is carried on a two wheel trailer along with an electrical generating unit; the hospital vehicle can be made ready for full operation within thirty minutes. Sufficient room is provided for operating teams composed of surgeons, nurses and technicians, making it possible for 2 men to be operated on simultaneously. The unit is capable of caring for from 80 to 100 men a day. The truck is equipped with a variety of special instruments for orthopedic, nerve, chest, maxillofacial and brain surgery; operating tables, steam and dry sterilizers, lighting equipment, medicines, blood plasma, bandages and dressings, record files, auxiliary power unit, surgical linens and operating gowns.

MAJOR DUNN APPOINTED NEUROPSYCHIATRIC CONSULTANT

Major William Harold Dunn has been appointed neuropsychiatric consultant for the Fifth Service Command Headquarters, Columbus, Ohio. Major Dunn was instructor in psychiatry at Cornell Medical College and assistant chief of the outpatient department at the Payne-Whitney Clinic in New York City. He has had extensive army experience with hospital units in the South Pacific. Immediately preceding his appointment he was on the staff of the School of Military Neuropsychiatry at the Mason General Hospital. Dr. Dunn graduated from Harvard Medical School in 1927.

NURSES DECORATED FOR GALLANTRY UNDER FIRE

Twelve officers of the Army Nurse Corps have been awarded the Bronze Star for heroic service in Italy, the War Department recently announced. This brings to 17 the number of American nurses who have been decorated for gallantry under fire. One Bronze Star and four Silver Star awards were made earlier.

CANCEL REQUISITION FOR PARASITOLOGISTS

Release FR-208, dated August 10, from the Headquarters Army Service Forces, Washington 25, D. C., states that the files of a sufficient number of qualified candidates have been received to meet the needs of the Surgeon General under requisition 228, parasitologists. This requisition will be canceled and further procurement will close immediately. Papers on candidates already procured and in process will be completed with the exception of WD AGO form 63, if not already accomplished, and forwarded under form OPS-22 with such requisition number shown in proper place.

CHIEF ARMY NURSE OF SIXTH CORPS AREA RETIRES

Lieut. Col. Pearl C. Fischer recently retired as chief of army nurses for the Sixth Service Command and was honored at a dinner at the Gardiner General Hospital, Chicago, August 8. Colonel Fischer was the first woman with that rank to serve with the Sixth Service Command. She will be succeeded by Lieut. Col. Martha Jane Clement, director of army nurses in the Southwest Pacific Area.

MAJOR MARY C. WALKER GIVEN HONORARY DEGREE

The University of Denver recently conferred the honorary degree of Doctor of Humane Letters on Major Mary C. Walker of the Surgeon General's Office. Mr. Thomas A. Dines, chairman of the board of trustees of the University of Denver, stated that "the university is pleased to extend this honor to a member of the nursing profession not only in recognition of her individual worth but as a fine representative of her profession."

SIXTY-NINE ARMY NURSES HAVE DIED IN LINE OF DUTY

The War Department recently announced that of approximately 40,000 members of the Army Nurse Corps 69 have lost their lives in line of duty since Pearl Harbor, 24 have been reported as wounded and 66 are prisoners of war. Six officers of the Army Nurse Corps have died as a direct result of enemy action. Other deaths have been due to vehicle accidents, airplane crashes and disease.

CHICAGO NURSE RECEIVES AIR MEDAL

Lieut. Helen F. Lyon of Chicago, a member of the first overseas flight nurse team, who went to the Aleutian theater last year to evacuate men wounded in the Attu campaign, has recently been awarded the Air Medal. With Lieutenant Lyon's unit when it arrived in the Aleutians was 2d Lieut. Ruth M. Gardiner, who was the first air evacuation nurse to lose her life in this war and after whom the Gardiner General Hospital was named.

FLIGHT SURGEONS' ASSISTANTS

A class of forty flight surgeons' assistants completed the six weeks course in aviation medicine at the School of Aviation Medicine, Randolph Field, Texas, July 29. These men are trained as specialists in assisting flight surgeons in the selection, care and maintenance of the flier. Brig. Gen. Eugen G. Reinartz is commandant of the School of Aviation Medicine.

FRENCH OFFICER CITED BY U. S. ARMY

Gen. Georges André Hugonot, Medical Corps, French army, was cited July 21 by the commanding general of the Fifth Army, U. S. He was serving as corps surgeon of the French Expeditionary Corps on the Italian front.

ARMY AWARDS AND COMMENDATIONS

Brigadier General Edgar Erskine Hume

Brig. Gen. Edgar Erskine Hume was recently awarded the Oak Leaf Cluster to the Distinguished Service Medal in recognition of service as chief of the Allied Military Government Section, Fifth Army, in Italy. The citation accompanying the award read:

"From Oct. 1, 1943 to Dec. 15, 1943, as chief of the Allied Military Government Section, Fifth Army, he successfully carried out one of the most extensive military government tasks ever accomplished by the United States, being charged with the government of Campania, a region of 6,000,000 inhabitants including Naples, one of Italy's largest cities. He made detailed plans for the administration of Naples, which, under his orders, were put into immediate execution when the city was taken on Oct. 1, 1943.

"Despite enormous handicaps in Naples, where the Germans had destroyed the water supply, electric power sources, drains and other public utilities, had mined buildings, despoiled hospitals, dispersed the police and in general paralyzed the civil administration, he was able by his unusual ability and devotion to duty to restore order forthwith and within a few weeks to return the city's functions almost to normal. A threatened epidemic of typhoid was averted by his wise preventive measures. Our victory was thus hastened, as the army commander was free to perform purely military functions without the added burden of civil government.

"The respect in which this officer was held by the Italians, his intimate knowledge of the country, its people and language, and his rare administrative skill and leadership made him unique in his efficient handling of an extremely difficult and politically delicate task."

General Hume was awarded the Distinguished Service Medal for his outstanding service as a medical officer during World War I as commissioner of the American Red Cross after the war in Serbia. He holds many decorations from foreign governments and numerous academic degrees from American and foreign institutions of learning.

General Hume graduated from Johns Hopkins University School of Medicine, Baltimore, in 1913 and was commissioned as a first lieutenant in the Medical Corps, Regular Army, Jan. 14, 1917.

Colonel Russell J. Caton

Col. Russell J. Caton, formerly of Bucyrus, Ohio, has received the Bronze Star for meritorious service at Guadalcanal, Solomon Islands, from May 13, 1943 to April 26, 1944. The citation reads "As island surgeon, Colonel Caton supervised and controlled medical service for thousands of troops at that base. In the supervision and coordination of twenty dispensaries and eleven hospitals he displayed unusual organizational ability, professional knowledge and leadership. He was directly responsible for the supply, storage and transport of medical equipment and supplies for operations on Guadalcanal and throughout the entire forward area. Under the expert guidance and force of purpose of Colonel Caton, the base medical service was developed to a widely extensive and efficient structure capable of meeting every exigency created by tropical climate and combat conditions. His careful planning and unerring sound judgment exemplify the highest tradition of the medical corps." Dr. Caton graduated from Ohio State University College of Medicine, Columbus, in 1913 and entered the service Feb. 1, 1941.

Colonel Frank B. Wakeman

The Legion of Merit was awarded posthumously to Col. Frank B. Wakeman, formerly of Indianapolis, for his meritorious work in connection with the training program of the Army Medical Department. The citation accompanying the award reads "For exceptionally meritorious conduct in the performance of outstanding services from July 1940 to March 1944. Colonel Wakeman, with rare foresight, initiative and organizing ability, laid the groundwork for the necessary expansion in all phases of Medical Department training, placing in operation replacement training centers, service schools for officers, Medical Department enlisted technicians schools and an officer candidate school long before the entry of the United States into the war. As a result of his insight into medical requirements and the execution of plans, the Medical Department was able to expand greatly its training activities following Dec. 7, 1941 and also, because of the training already given, to render an efficient medical service to the Army during the very rapid expansion that followed the declaration of war. Colonel Wakeman's unusual foresight, aggressive execution of approved plans and selfless devotion to the best interests of the Army and the Medical Department are in the highest traditions of the service." Dr. Wakeman graduated from the Indiana University School of Medicine, Indianapolis, in 1926. The Association of Military Surgeons awarded him the Henry Wellcome Prize in 1938 for his thesis on an immunizing antigen of the typhoid bacillus.

Colonel John A. Rogers

Col. John A. Rogers, Army Medical Department, formerly on duty in Washington, D. C., as executive officer of the Office of the Surgeon General, has been awarded the Legion of Merit for services in the European theater. The citation stated that the award was given for "exceptionally meritorious conduct in the performance of outstanding services from Oct. 20, 1943 to May 31, 1944." Dr. Rogers graduated from Tufts College Medical School, Boston, in 1914. He was formerly a member of the New Hampshire National Guard and entered the Medical Corps of the Regular Army in 1933, serving at posts in this country and in Hawaii.

Captain William I. Hunt

Posthumous award of the Silver Star Medal was recently made to Capt. William I. Hunt, formerly of Greenville, Miss., for gallantry in action. The citation accompanying the award read "Desiring to be where he was needed most, Captain Hunt accompanied a small reconnaissance patrol into Japanese territory. The patrol ran into an enemy ambush, which opened fire at a 30 yard range. During the action the lead scout was killed and three other men were wounded. Captain Hunt, disregarding his personal safety, courageously went forward under exposure to the heavy hostile fire toward the casualties and in doing so was mortally wounded. Although such bravery was neither ordered nor expected, this officer readily sacrificed his life in an attempt to help his wounded comrades." The organization to which Dr. Hunt belonged, the American Division, was the first army division to participate in offensive action in this war. Named for American forces in New Caledonia, where it was activated, it fought at Guadalcanal and is the only division officially with a name instead of a number. Dr. Hunt graduated from Tulane University of Louisiana School of Medicine, New Orleans, in 1942 and entered the service June 30, 1943.

Captain Ralph S. Phelan

The Silver Star award was recently given to Capt. Ralph S. Phelan, formerly of Waurika, Okla. The citation accompanying the award read "On Nov. 22, 1943, in the Mediterranean theater, he was battalion surgeon of an infantry battalion which was occupying a defensive position on a mountain top. Enemy artillery caused many casualties, and the rugged terrain made evacuation almost impossible. He went up the side of the mountain and administered first aid to the wounded in the battle area. His action under fire was credited with saving many lives." Dr. Phelan graduated from the University of Oklahoma School of Medicine, Oklahoma City, in 1939 and entered the service July 1, 1941.

Captain Andrew J. Extejt

The Bronze Star Medal was recently awarded to Capt. Andrew J. Extejt, formerly of Toledo. Dr. Extejt was decorated for military operations against the enemy in Normandy June 7-10. He has been overseas for more than a year and also saw action in Africa, Sicily and Italy. Dr. Extejt graduated from St. Louis University School of Medicine in 1934 and entered the service Aug. 27, 1942.

NAVY

NAVY AWARDS AND COMMENDATIONS

Captain Lockhart D. Arbuckle

Capt. Lockhart D. Arbuckle, now senior medical officer at the Naval Training Center, Great Lakes, Illinois, has been awarded the Legion of Merit "for exceptionally meritorious conduct in the performance of outstanding services to the government of the United States as division surgeon of a Marine division during the planning for and the operations against the Japanese on Bougainville, British Solomon Islands, from Sept. 10, 1943 to Jan. 4, 1944. During this period Captain Arbuckle rendered invaluable assistance to the commanding general in executing the operation under the most adverse conditions. When the preparations for the establishment of the beachhead were begun, owing to his highly efficient supervision of the medical facilities all troops entered the combat areas in excellent physical condition. As a result of his exceptional professional skill and constant attention to duty, medical services were administered to all the wounded, and despite the trying conditions arising from tropical climate, losses from sickness and battle wounds among the troops were held to a minimum. His superior knowledge and sound judgment contributed materially to the success of the campaign and were in keeping with the highest tradition of the United States Naval Service." Dr. Arbuckle graduated from the Medical College of Virginia, Richmond, in 1915 and has been in the service since May 28, 1917.

Lieutenant Commander Richard Monroe Forsythe

Posthumous award of the Navy Cross has been made to Lieut. Comdr. Richard Monroe Forsythe, formerly of Cleveland. The citation accompanying the award read "For extraordinary heroism while serving as regimental surgeon with the . . . First Marine Division, during action against enemy Japanese forces near Volupai Plantation, Willaumez Peninsula, New Britain, on March 6, 1944. When our forces suffered severe casualties while landing on the strongly fortified beach, Lieutenant Commander Forsythe immediately went to the assistance of the wounded and, undeterred by devastating hostile mortar fire, untiringly administered medical aid to the injured and assisted in moving them out of range of Japanese guns. Courageously remaining in the exposed area despite multiple wounds from a bursting enemy mortar shell, he continued ministering to the injured until severe pain finally forced him to cease his valiant efforts. Although fully aware that postponed surgical attention would gravely impair his chance of recovery, Lieutenant Commander Forsythe steadfastly refused medical assistance while there were other casualties in need of care and later succumbed as a result of wounds received in this action. His outstanding professional skill, his great personal valor and heroic devotion to duty were an inspiration to his associates and reflect the highest credit on the United States Naval Service. He gallantly gave his life for his country." Dr. Forsythe graduated from Western Reserve University School of Medicine, Cleveland, in 1937 and entered the service May 31, 1940.

MISCELLANEOUS

MORE THAN 400 FROM POST-GRADUATE HOSPITAL NOW SERVING WITH ARMED FORCES

More than 400 physicians, nurses and others connected with the Post-Graduate Hospital, New York City, are now serving with the armed forces. The number of physicians attached to the Army, Navy and Marines in various battle fronts is one of the largest from any hospital in the country. Doctors from the attending staff of the hospital number 296, while there are 47 from the intern and resident units. In addition to these there are 47 nurses, who, like the doctors, are volunteers. One member of the hospital staff has been killed in action, and those drafted from the nonvolunteer group have reached a total of 36.

The Post-Graduate veterans now in uniform will often be reminded of their home service by the fact that they will use some of the flying ambulances for the transfer of their patients. Owing to the success of the "E bond" campaign conducted at the hospital, three of these great air ambulances will carry the name of the Post-Graduate Medical School and Hospital.

The medical school is engaged in arrangements for classes and courses for military doctors returning to their civilian practices, scores of whom have asked for this training.

RESTRICTIONS ON USE OF AGAR REMOVED

The War Production Board recently announced that stockpiles of agar, formerly dependent on supplies received exclusively from Japan, have now been improved to such an extent by newly developed domestic production and by imports from Mexico that restrictions on the use of agar have been removed, by revocation of Order M-96. Agar, a jelly-like substance extracted from certain types of seaweed found on both the Atlantic and Pacific coasts, is principally used in making bacteriologic cultures, but only the seaweed found on the West Coast yields the type of agar that can be used for the production of these cultures. Agar is also used in the preparation of medicinals, pharmaceuticals and food, and in the drawing of tungsten wire and the manufacture of dental impression compounds.

Domestic production of agar was accomplished as a result of close cooperation between industry and the Chemicals Bureau of the War Production Board. The largest agar plants, the American Agar and Chemical Company, is situated in Los Angeles. Smaller agar production units have been established in Massachusetts, the Carolinas and Florida.

To insure fulfilment of any emergency needs for agar, a stockpile is being reserved by the Defense Supplies Corporation, a subsidiary of the Reconstruction Finance Corporation.

HOSPITALS NEEDING INTERNS AND RESIDENTS

The following hospitals have indicated to the Council on Medical Education and Hospitals that they have not completed their house staff quota allotted by the Procurement and Assignment Service:

(Continuation of list in THE JOURNAL September 2, page 37)

CALIFORNIA

Santa Clara County Hospital, San Jose. Capacity, 470; admissions, 4,435. Dr. Henry E. Dahleen, Superintendent (resident—tuberculosis).

KENTUCKY

Louisville General Hospital, Louisville. Capacity, 587; admissions, 9,805. Dr. John W. Moore, Medical Director (1 intern, 1 assistant resident—medicine, October 1).

MICHIGAN

Leila Y. Post Montgomery Hospital, Battle Creek. Capacity, 165; admissions, 6,301. Sister Mary Constance, Administrator (intern).

NEW YORK

Israel Zion Hospital, Brooklyn. Capacity, 380; admissions 10,532. Dr. J. Praeger, Executive Director (interns, October 1944, January 1945).

RHODE ISLAND

Butler Hospital, Providence. Capacity, 175; admissions, 178. Dr. Arthur H. Ruggles, Superintendent (residents—psychiatry).

TEXAS

All Saints Episcopal Hospital, Fort Worth. Capacity, 100; admissions, 3,997. Miss Eva M. Wallace, R.N., Superintendent (resident—mixed).

WISCONSIN

Methodist Hospital, Madison. Capacity, 127; admissions, 3,911. Miss Carolyn M. Fenby, R.N., Superintendent (interns).

URGE SPECIAL MICROSCOPIC TESTS BEFORE TREATING GONORRHEA WITH PENICILLIN

Dr. C. J. Van Slyke of the Public Health Service Venereal Disease Research Laboratory, Staten Island, N. Y., and Dr. S. Steinberg of the U. S. Marine Hospital, New York City, recently reported the possibility of overlooking syphilis symptoms in gonorrhea patients treated with penicillin in patients who have both diseases. This can be avoided, however, if special microscopic tests are made before penicillin is used, and if blood tests are made after penicillin treatment has been completed. The masking effect of penicillin on syphilis symptoms is due to the fact that the relatively small amounts of penicillin required to cure gonorrhea are sufficient to cause disappearance of the spirochete germs of syphilis from syphilis lesions, although not sufficient actually to cure syphilis. When serum from the lesions is examined under a special microscope after penicillin has been used, the spirochetes will not be seen, and the examining doctor may be misled to conclude that the patient was not infected with syphilis. Making the microscope examination before treatment with penicillin prevents this possible error. A blood test for syphilis some time after the treatment of gonorrhea has been completed is advisable, because blood tests do not always reveal very new syphilis infections immediately after they have been acquired.

MEDICAL AND SURGICAL RELIEF COMMITTEE OF AMERICA

The Medical and Surgical Relief Committee of America (420 Lexington Avenue, New York City) recently donated a shipment of medical supplies, including five cases of fracture pillows, crutches, stretchers, wheel chairs and a fracture cradle for use of wounded soldiers, to the Halloran General Hospital, Staten Island, N. Y. The Medical and Surgical Relief Committee of America was organized four years ago and is conducted by a nationwide group of physicians, surgeons and dentists. The committee is a philanthropic organization dedicated to medical, surgical and dental aid for the armed and civilian forces of the United Nations. To date the committee has shipped and delivered safely in America more than $640,000 of supplies.

PRINTED FORMS FOR CADET NURSES WHEN TRAVELING

Some members of the U. S. Cadet Nurse Corps have encountered transportation difficulties through being confused with members of the armed forces. In one instance a cadet nurse was unable to purchase a train ticket because a passenger agent, thinking her a member of some governmental service, requested to see furlough papers, which of course she did not have. This occasioned an expensive delay in her trip. In order to avoid this possible confusion the U. S. Public Health Service is printing forms which will be sent in the near future to directors of schools of nursing which (when signed) are to be given to cadet nurses who are traveling in uniform. This will clarify the situation for any agent who, in line of duty, might question their right to travel. Additional forms will be sent to the directors of schools of nursing on request.

COMMITTEE ON MEDICAL RESEARCH BEGINS PUBLICATION

The Committee on Medical Research of the Office of Scientific Research and Development began publication recently of a weekly journal entitled *Summary of Reports Received by the Committee on Medical Research.* Circulation of the publication is restricted to selected Medical Corps men in the United States, Canada and Great Britain. The journal is being edited and published by the records section of the committee, the work of which is directed by Dr. Kenneth B. Turner, who is on leave of absence from Columbia University College of Physicians and Surgeons.

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

At Camp Ellis, Illinois: Conditions Affecting Glucose Metabolism, Drs. Arthur R. Colwell and George W. Scupham, September 20.

At Camp Grant, Illinois: Recent Advances in the Treatment of Syphilis, Drs. Robert M. Craig and George X. Schwemlein, September 20.

At Chanute Field, Rantoul, Ill.: Chemotherapy—Present Status, Drs. W. Barry Wood Jr. and Italo F. Volini, September 20.

HEALTH NEWS FROM EUROPE

According to DNB of May 13, 1944 (Germany) hospitals have time and again been the target of enemy terror bombers. Far sighted vision revealed many years ago the need for sick persons to be lodged outside towns, in a place where they would be safe from air attacks. Prof. Dr. Brandt, the führer's general commissioner for the medical and health services, was entrusted by the führer with the task of devising and applying the necessary measures. Under the technical direction of Dr. Poschmann, delegate of the general commissioner for hospital emergency installations and of Ministerial-Direktor Schönleben of the building office in the Speer ministry, emergency hospitals were built in several stages at many places all over the reich. Although they are in the nature of emergency hospitals they combine all the qualities of an up to date hospital building with the added advantage of being close to nature, which is particularly beneficial to the sick and also affords protection from air attacks.

Reich Minister Speer gave press representatives an opportunity to inspect such a hospital which is under construction in the neighborhood of the reich capital. The friendly and airy rooms with their white ceilings make one oblivious of the fact that they are really hutments. In planning the site the "pavilion" system was abandoned and the six wards form a close structure; they are connected by a 250 meter brick corridor, which makes it possible to move within the hospital, regardless of temperature and weather, exactly as in the several floor building of the town hospital. Each ward consists of several fair sized sickrooms with 6 to 8 beds each, while the smaller sickrooms, wash rooms and bath rooms and a cozy common room are situated on the other side of the passage. In each ward there is room for the offices of the doctors and sisters and a kitchenette on the other side of the main connecting corridor. A modern central kitchen for the whole hospital is situated at one end of this corridor, while at the other end is the ward for infectious diseases, which is completely isolated from the other wards and in its design is probably the most up to date of its kind in Europe. Situated between the wards exactly in the center of the whole site is the reception and treatment hut, which also houses the x-ray units and the laboratory and contains the consulting rooms of the dentist, the ophthalmologist and other specialists.

Many such hospitals were completed in the neighborhood of many air raid danger towns during the last four months; despite wartime difficulties it was possible to complete the buildings in the short space of six to eight months. Each hospital has 500 beds and in an emergency will hold as many as 800. Germany disposes already of 15,000 such beds, while space is being provided for thousands more. New methods are also being employed in the administration of these emergency hospitals. They are under the direction of General Commissioner Dr. Brandt, to whom the senior house surgeon is responsible in all matters. This procedure eliminates red tape, particularly in questions of hospital supplies and also in the admission of patients; they are treated there regardless of who is to pay.

These hospitals will naturally be used in the first place to house serious cases and others which it will take some time to cure, while the hospitals in the towns will continue to be available for day to day cases.

The Netherlands Information Bureau states that a group of prominent physicians recruited from American medical schools and hospitals will leave for the Netherlands after that country's liberation to give a series of four week postgraduate refresher courses in Dutch universities. This plan was announced by Dr. Herbert Loeb of Cambridge, Mass., former president of the Netherlands Dental Association at Amsterdam, who was instrumental in arranging for a similar postwar movement to bring dental care to the Netherlands. Nine medical specialists will make the transatlantic voyage to give the refresher courses, which cover eight specialties and have been prepared in both the English and the Dutch languages. The Netherlands government will finance the traveling and other personal expenses of the American professors, who will, however, receive no extra or special compensation for their work in the Netherlands. Because of German looting of Dutch medical schools and hospital equipment, the physicians will take with them all material and instruments needed for laboratory and demonstration purposes.

The idea of these refresher courses originated with Dr. Herman deJong of Duke University, formerly of the University of Amsterdam, where he specialized in neurology and psychiatry for the Dutch branch of the Rockefeller Foundation. He discussed his plan with Dr. Gerrit Bolkestein, Netherlands minister of education, when the latter toured a number of American universities last May, who approved the plan. In addition to Dr. deJong, the expedition will include Dr. Frederick M. Hanes, clinical medicine; Dr. Keith S. Grimson, surgery; Dr. David T. Smith, bacteriology and infectious diseases; Dr. Edwin C. Hamblen, obstetrics, gynecology and hormonology, all of whom are from Duke University School of Medicine, Durham, N. C.; Dr. Wilburt Davison, dean of Duke University School of Medicine, pediatrics. Dr. Isidore Snapper, director of the Department of Graduate Medical Education at Mount Sinai Hospital, New York, will also cover clinical medicine. Dr. Snapper left the University of Amsterdam in 1937 to go to the Rockefeller Foundation at Peiping, China. He was captured by the Japanese and later sent to America as an exchange prisoner. Other members are Dr. C. J. Van Slyke of the Rockefeller Institute, New York, biochemistry, and Dr. Eli K. Marshall Jr., Johns Hopkins University, physiology and pharmacology.

According to *Le journal* of May 18, diets for sick people are granted only on production of a medical certificate drawn up on a printed and numbered form delivered monthly for three periods of ten days. The control is severer as regards No. 1 and feeding up diets, which are granted with the greatest parsimony for only five, seven and sometimes ten days. Each doctor now receives, through the medical council, five printed forms per thousand inhabitants of his district. Thus a skin or eye specialist is entitled to prescribe the same number of diets as a child specialist, whose patients need most feeding up. The results of this measure were that in one Lyons arrondissement the number of persons entitled to diet No. 2 fell within a month in the proportion of four to one. Under diet No. 2 the meat, cheese and wine rations can be replaced by 0.25 liter of milk daily and 750 Gm. of spaghetti, 750 Gm. of sugar and 6 Kg. of potatoes monthly. Those entitled to this diet are generally old persons unable to eat the present meat, and for whom doctor's fees are often an extravagant expenditure which they cannot afford to repeat monthly, preferring to give up the diet. It is incomprehensible that certain patients cannot be treated because the doctor has used his five diet vouchers. Thus the district doctor is often compelled to deprive of their diet those who need it most.

According to *Der Bund*, Berne, of June 28 it is not known whether the decision of the French medical council whereby no doctor may leave the Paris region without the permission of the council is connected with the communiqué extending the compulsory labor service to doctors, or whether it is merely intended to prevent the regrettable situation which arose in the summer of 1940 owing to the mass flight of doctors. The council's circular adds information about the difficulties facing the medical profession owing to the restrictions on electricity and gas in the Paris district. X-rays can no longer be used either in hospitals or in private consulting rooms. It is almost impossible to sterilize instruments. The modest supplementary distribution of methylated spirit is inadequate.

DNB of May 15, 1944 (Germany) states that the penal regulations on professional abortion have been tightened up by the order for the protection of marriage, family and motherhood. The penal code now provides for the death sentence in cases in which the vitality of the German people has been impaired by continuous abortion. The special court at Frankfurt on the Oder applied this new provision of the law against Heinrich Schulz of Balkow, Kreis West-Sternberg. Schulz had carried out altogether nine abortions and thus committed a particularly grave sin against the future of his people. He was sentenced to death as a dangerous habitual criminal for professional abortion. The sentence has already been carried out.

The DAF announced that five hundred theater performances and lectures were held for Dutch workers in Germany in April, according to the German European Service of May 24, 1944. Medical care for foreign workers in Germany has been further improved. Three hospitals in central Germany have been opened exclusively for their use equipped with the most modern installations, special departments for infectious diseases and clinics for women. Doctors and nursing staff are recruited from Germany and many European countries.

SNP (Norway) reports, according to *Aftontidningen*, Stockholm, of June 21 that a number of young Oslo girls were recently conscripted for "national labor service" in German military hospitals in Oslo and the surrounding districts. The Norwegian home front boycott of conscription included such conscriptions, and if the German authorities continue to summon Norwegian girls, then the girls may find themselves in the same situation as men conscripts.

The Chambery medical board, considering the prohibition of night automobile traffic, the substantial fuel reduction and telephone restrictions, earnestly asks patients to abstain from calling doctors at night, since it is virtually impossible to travel after 10 p. m., according to *Le Nouvelliste de Lyon* of June 17. The most distant patients can be visited only in daylight by taxi.

Transocean (for the Far East) of May 12, 1944 (Germany) states that the first bomb proof dispensary has been opened in a Ruhr town. Built into a steep slope, it is 13 meters long but only 3 meters wide and 2.8 meters high. Ten cupboards contain 5,000 types of drugs and medical supplies, sufficient to meet four weeks' requirements.

Radio Paris of May 22 reports from Brussels that during the night of May 19 a large quantity of anesthetic drugs was stolen by unknown persons from a depot of pharmaceutical products, including a large quantity of crude morphine destined for hospitals and clinics. The stolen goods are valued at about 2 million francs.

The minister of the interior, according to *Slovo* of March 3, 1944, has signed an order published in the Official Gazette of March 24 stating that the fees paid in private hospitals and sanatoriums in the country are increased by 100 per cent over what they were in 1936.

The Mulhauser *Tagblatt* for April 20 (Alsace) states that by a decree dated March 4 (published in the Verordnungsblatt des Chefs der Zivilverwaltung im Elsass of April 4) the law introduced in the reich on July 14, 1933 for the prevention of hereditary disease in the rising generation is now valid in Alsace.

ORGANIZATION SECTION

WASHINGTON LETTER

(From a Special Correspondent)

Sept. 4, 1944.

Hearings on Blindness and Infantile Paralysis

Sixty per cent of the cases of blindness in this country are unnecessary and could be prevented, Dr. Harry S. Gradle, professor of ophthalmology at the University of Illinois College of Medicine and vice president of the Illinois Society for the Prevention of Blindness, testified here this past week before the Kelley Labor Committee Subcommittee to investigate aid to the physically handicapped. He spoke as a representative of the American Medical Association. Dr. Gradle deplored the fact that there are not sufficient agencies where a newly blinded person can become accustomed to his affliction and get training in new uses of his senses and capabilities. He suggested centers such as those now operated by the Army and Navy for reconditioning men blinded in war. Prevention of blindness, he contended, "is of even greater importance than care for the blind."

Dr. Gradle recommended that state public assistance commissions be assisted in the physical rehabilitation of the blind. "There are enlisted," he said, "6,000 ophthalmologists in the United States, of whom a little over 2,000 have been certified as being ophthalmologists and 2,000 who are doing capable work without certification. The other 2,000 comprising the 6,000 are mostly general practitioners who are doing a small amount of ophthalmology on the side but who are not capable of doing necessary rehabilitation work." He explained later that "the number we have is sufficient for the physical rehabilitation of the blind. The 6,000 in existence are not enough to cover the needs of the general population of the United States, apart from rehabilitation."

Dr. Gradle was followed as a witness by Dr. Allan C. Wood, director of the Department of Ophthalmology in Johns Hopkins University School of Medicine and director of the Wilmer Ophthalmological Institute, who expressed the opinion that the Sanders 1934 estimate of 150 blind persons per hundred thousand, or from 215,000 to 240,000 blind in the United States, was most accurate of all estimates and "a fair guess." He quoted National Health Survey figures on the incidence of blindness in the 100,000 of population, as follows: "You will find that 11 per hundred thousand of the population are blind under 15, and that figure steadily goes up, so that for the ages between 45 and 54 you find that 90 per hundred thousand are blind, and when you get to 75 to 84 you find that approximately 1,000 per hundred thousand are blind, and when you get to 85 plus, practically 3,000 per hundred thousand of the population are blind. The answer to that is that the people are moving in their advancing age to the time when the various diseases take their toll of blindness."

These two witnesses were among a score or more heard by Representative Augustine B. Kelley (Democrat, Pennsylvania) in the study on blindness. During the present week it is proposed to hear experts testify regarding the prevalence of infantile paralysis to determine if adequate facilities are available for its treatment. The purpose of the hearings, according to Representative Kelley, is to "learn the causes of the handicaps and the means to cure or alleviate them, to provide the afflicted with educational opportunities, training and restoration to gainful occupations, and to assist those who cannot be employed."

Postwar Hospitalization Under Study

Favorable indications for the bill providing federal aid to build a cooperative hospital center in Washington, to be operated on a self-sustaining and nonprofit basis, have stirred interest here generally in United States postwar hospitalization needs. Senator Millard Tydings (Democrat, Maryland), one of the chief sponsors of the bill, has expressed the conviction that Congress would approve the plan, in which participating hospitals here would pool their resources to carry the full load of maintenance costs. He emphasized that Congress was not expected to contribute anything toward the annual expenses.

The pending plan calls for construction of a 1,500 bed hospital center in which any of Washington's private hospitals could join as participating or associate members. The cost is estimated at between $6,000,000 and $7,500,000 exclusive of land. To date only Garfield and Emergency hospitals have decided to join the center as full participating members.

Health authorities here have shown interest in what has been done by the Cleveland Hospital Service Association to help people meet the cost of illness without leaning on the government for funds or control. Eight hundred thousand people in the greater Cleveland area are entitled to benefits, with 55 per cent of all the residents of the community enrolled in the service and currently adding 100,000 additional subscribers annually. Each subscriber to the association makes a small monthly payment, which insures him or a member of his family of proper hospital care when necessary. In its ten years of existence the association has provided such care for 300,000 patients. The Cleveland Hospital Service Association, one of the pioneer organizations of its kind, provides hospitalization only and does not include services of the physician or surgeon. It is one of seventy-eight such associations operating in the United States, details of operations differing in various communities.

MEDICAL ECONOMIC ABSTRACTS

CALIFORNIA PHYSICIANS' SERVICE

A REPORT BY THE BUREAU OF MEDICAL ECONOMICS

The California Physicians' Service has just issued its fifth annual report, so comprehensive as to various phases of the operation of the plan as to form an excellent guide to other state and local medical associations considering the establishment of a prepayment plan. As the first statewide plan, California has been forced to experiment in many directions. It has issued several types of contracts. It still retains a number of these as suited to special conditions. Its largest enrolment is now under the surgical service contract, in which membership dues per month are $0.60 for male employees, $0.90 for female employees, $1.50 for an additional dependent and $2.25 for two dependents. Participation is limited to those with incomes under $3,000 a year, to whom all contracted services are granted.

Employed beneficiary members under the surgical contract may obtain a "two visit deductible medical rider." With a few exceptions this covers a complete medical service for the payment of 75 cents a month in addition to the regular surgical contract rate. To meet the demand for those with an income of more than $3,000 an indemnity surgical reimbursement contract is issued under which patients make their own arrangements with physicians and receive reimbursement under the regular schedule of the surgical contract.

In northern California territories California Physicians' Service has found it necessary to cover hospitalization as well as surgical services. The hospital rider rates per month are 75 cents for the employed man, 80 cents for the employed woman and $1.80 and $2.40 for one and two or more dependents respectively.

Service is also furnished for farm families with an income of less than $2,000 a year. This program, conducted in cooperation with the Farm Security Administration, provides for medical, surgical and hospital care to all members of the family alike. A fee of $1.50 must be paid by the patient for the first home visit, and there are some other minor limitations. The rates annually are $30 for single persons, $48 for a family of two and $60 for a family of three or more.

As a special war emergency undertaking, the California Physicians' Service entered into contracts to provide medical, surgical and hospital care to residents of projects under the jurisdiction of local housing authorities. Monthly rates were $2.50 for single persons, $4 for a family of two and $5 for larger families.

The experience with the Rural and Housing Project contracts has gained a necessary knowledge of methods of cooperation with government bodies as well as of the variations in service required under these different conditions. At present California Physicians' Service is paying 90 per cent of what might be called the normal unit value. At one time in 1940 the amount paid per unit was $1.10 and in February 1944 it was $2.25. In the meantime the "unit state fund" has been increased to $70,000. It is hoped that this backlog will avoid such violent fluctuations in the future. While fairly good relations have been established with such diverse bodies as labor organizations, membership served, hospitals and government agencies, the relations with the medical profession, etc., still remains "the most urgent problem of C. P. S. . . . Without an active and positive support from its professional members, C. P. S. cannot grow, and if it cannot grow it will never reach its true value to the medical profession. C. P. S. is an agency composed of its professional members. It must, regardless of the personal desires of individuals, function as the bulk of its members wish. It cannot perform its purposes in any other manner. . . .

Many of the problems of acquisition are directly related to the lack of professional member support and the lack of labor and employer support.

DISCUSSIONS ON POSTWAR SECURITY

National Health Plan Advocated by Dr. Parran

The United Press reports that a postwar national health program, supported by insurance and taxation, was proposed by Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service, in a Labor Day address at the University of California medical center, San Francisco. He suggested that the program should not be "entirely socialized or an entirely private undertaking but a combination of both."

Health Plan Offered to Workers in East

According to the United Press, incorporation papers for a health insurance plan covering all persons living or working in New York and earning not more than $5,000 annually have been filed with the state board of social welfare and the superintendent of insurance. The plan, providing medical and surgical care, is expected to be ready for operation by January 1, with most of the city's 190,000 employees and many union members enrolled, Mayor F. H. LaGuardia announced. Incorporators include Henry J. Kaiser, West Coast shipbuilder; former Governor Alfred E. Smith, and Beardsley Ruml, chairman of the board of the Federal Reserve Bank; Gerard Swope, chairman of the board of the General Electric Company, Sidney Hillman, president of the Amalgamated Clothing Workers Union; Wendell Willkie, and the borough presidents.

Eric Johnston Speaks

According to the Chicago *Tribune*, high praise for America's private security system of insurance as compared with any "incentive stifling burocracy" contemplated in a postwar superfederal social security system was given by Eric Johnston, president of the Chamber of Commerce of the United States, in an article which will appear in the forthcoming issue of the *Casualty and Surety Journal*. "The private security system of insurance is as American as apple pie," Johnston wrote, "for it was conceived and developed in the adventurous American spirit of individual initiative and enterprise. No sprawling, incentive stifling burocracy is this dynamic system, but a nationwide industry, composed of 524,000 self-reliant employees and producers earning their own way in the world, keeping in step with the pulsating tempo of progress." Johnston said that, through private enterprise, a supersocial security system is already here and questioned "the need of elaborate blueprints for a superfederal social security system."

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—The Kelley subcommittee of the House Committee on Labor has scheduled hearings for September 12, 13 and 14, at which time testimony will be received relating to the aid given to the hard of hearing and the deaf. H. R. 1506 has passed the House and Senate, and Senate amendments have been agreed to by the House, proposing to amend further the Pay Readjustment Act of 1942. This bill, among other things, will permit the counting of services in the Medical Reserve Corps for pay purposes. H. R. 5257 has been reported to the House, a bill to provide for health programs for government employees, with an amendment exempting the Tennessee Valley Authority from the scope of the bill. Health services now provided by any governmental agency will continue until June 30, 1945, at which time the Civil Service Commission in consultation with the United States Public Health Service will supervise such health activities.

Bills Introduced.—S. J. Res. 147, introduced by Senator Langer, North Dakota, would authorize an appropriation of $10,000,000 for the investigation and study of the origin, causes and means of control of infantile paralysis. This resolution proposes to create an Infantile Paralysis Control Board to be composed of the Surgeon General of the Public Health Service as chairman and one outstanding member of the medical profession in each state and in the District of Columbia to be appointed by the Surgeon General. The Surgeon General will also be authorized to "appoint Sister Kenny, the famed Australian nurse, as a member of the board." H. J. Res 305, introduced by Representative Priest, Tennessee, would authorize the Surgeon General of the United States Public Health Service to dispose of certain reserves of liquid, frozen or dry blood plasma or serum albumin to federal, state or local public health authorities or to federal or other nonprofit hospitals. This plasma or albumin is being held in reserve for casualties resulting from enemy action and disposition is to be made of it when the Surgeon General determines that it is no longer needed for the purpose for which it is held in reserve. H. R. 5249, introduced by Representative Rankin, Mississippi, contemplates an amendment to title II of the G. I. Bill of Rights, relating to the education and training of returning veterans, to provide that if any publicly supported institution or private institution exempt from tax under section 101(6) of the Internal Revenue Code has no established tuition fee, or if the established tuition fee is less than the actual cost to such institution of furnishing the education and training, the Administrator of Veterans' Affairs will be authorized to provide for the payment to such institution of the actual cost of furnishing education or training to a veteran, but not to exceed $500 for an ordinary school year.

DISTRICT OF COLUMBIA

Bills Introduced.—S. 2074, introduced by Senator Tydings, Maryland, for himself and Senator Bilbo, Mississippi, and H. R. 5183, introduced by Representative Harless of Arizona, propose to provide for the establishment of a modern, adequate and efficient hospital center in the District of Columbia. A subcommittee of the Senate Committee on the District of Columbia has conducted hearings on S. 2074. It is understood that the Medical Society of the District of Columbia has approved the bill in principle on condition that all nonprofit voluntary hospitals affording service to indigents and near indigents in the District be given equal opportunity to participate in the program and on condition that they be assured equal representation in the corporate body created by the bill, namely the Washington Hospital Corporation.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Symposium on Penicillin. — The San Francisco County Medical Society devoted its August 8 meeting to a symposium on penicillin at which the following participated:

Dr. Lowell A. Rantz, The Background of Penicillin Therapy.
Dr. Arthur L. Bloomfield, Special Problems in the Clinical Uses of Penicillin.
Drs. Horace J. McCorkle and Henry L. Silvani, Uses of Penicillin in Surgical Infections.
Comdr. Clark M. Johnson (MC), Uses of Penicillin in Infections of the Genitourinary Tract.

Course on Occupational Dermatoses. — Dr. Louis Schwartz, medical director of the dermatoses section of the U. S. Public Health Service, will conduct a course on occupational dermatoses at the Los Angeles County Medical Association, Los Angeles, September 18-23, under the auspices of the University of Southern California School of Medicine and the College of Medical Evangelists, the Los Angeles Chamber of Commerce and the Los Angeles County Medical Association.

Physician Wanted.—The Los Angeles County Civil Service Commission announces that a chief physician (tuberculosis) is wanted to administer the tuberculosis service of the Los Angeles County Hospital or to assist in directing medical care and treatment of patients at Olive View Sanatorium and to act as tuberculosis consultant. Physicians under 55 years of age who have an M.D. degree and three years' recent experience or training in the specialty of tuberculosis are urged to apply for this position, which carries a salary of from $417 to $489 a month. Full information and applications may be obtained from the office of the commission, Room 102 Hall of Records, Los Angeles 12. Applications must be filed on or before September 16.

DELAWARE

Committee for Postwar Planning. — The state medical society has appointed a committee of nine to be known as the Committee of Postwar Planning of the Medical Society of Delaware, composed of the following members: Drs. Richard C. Beebe, Lewes; Joseph B. Waples Jr., Georgetown; John Roscoe Elliott, Laurel, representing Sussex County; Joseph S. McDaniel, Dover; William Marshall Jr., Milford, representing Kent County; William O. LaMotte, William Edwin Bird, Frederick A. Hemsath, secretary, all of Birmingham, and Mesrop A. Tarumianz, Farnhurst, chairman, representing New Castle County. A survey of medical and hospital services of all types will be carried out in sections of the state to aid the committee in studying adequate medical services of various specialties for every community of the state, various hospital facilities, medical service to industry, large and small, adequate medical service of all types for public schools, the need for closer relationship between all existing state, municipal and private postwar planning organization and to enlist the full cooperation of all physicians and hospitals for rehabilitation of veterans. The society, which believes that as a scientific organization it cannot achieve the desirable level of success unless it becomes an integral part of the economic and social structure of the country, will cooperate with the state legislature, state administration, various boards of education, various industrial and agricultural organizations, chambers of commerce, bar association, state and municipal and private, social, civic and religious agencies, all labor unions promulgating the definite policy that sound health is the business of every citizen and the prerogative of progressive people, and that this can be achieved through the help and cooperation of organized medicine.

ILLINOIS

Stuart Wood Memorial Fund.—Plans are under way to establish a memorial fund in honor of the late Dr. Wilbur Stuart Wood, Decatur. The memorial will take the form of a fund to be used to purchase orthopedic equipment in the Decatur and Macon County Hospital, where Dr. Wood had been active for many years. Dr. Wood died August 7.

Chicago

Rongetti Sentenced to County Jail.—Amante Rongetti, whose license to practice medicine was revoked in 1932 when he was sent to the state prison at Joliet following his conviction of manslaughter, was sentenced August 30 to three months in the county jail for practicing medicine without a license and fined $500. Newspapers reported that the sentence was imposed by Judge Russell W. Keeney of Du Page County sitting in county court. Rongetti is also reported to have served a term in the federal penitentiary at Leavenworth for violating the federal narcotic act. At the trial, June 14, Rongetti was found guilty by a jury after an inspector for the state department of registration and education testified that he had prescribed distilled water for a "supposed kidney ailment." Ray E. Lane, Rongetti's attorney, said he would appeal.

Assembly on Nervous and Mental Diseases and War. —The Institute of Medicine of Chicago will hold its postgraduate assembly, November 1-2, at the Palmer House. The program will cover "Nervous and Mental Diseases and War" and will be devoted to phases of neurology, psychiatry and neurosurgery that are of particular importance to clinicians, specialists and lay workers. There will be a registration fee of $5 for all except those in uniform. Among the speakers will be:

Dr. Samuel W. Hamilton, Washington, D. C., Psychiatry Before World War II.
Dr. Winfred Overholser, Washington, Civilian Mental Health in Wartime.
Dr. C. Charles Burlingame, Hartford, Conn., Present and Future Effects of War Neuroses.
Dr. Bernard J. Alpers, Philadelphia, War and Nervous Disorders.
Dr. Cobb Pilcher, Nashville, Tenn., Civilian Advances and Investigations in Neurosurgery During the War.
Col. William C. Menninger, M. C., The Mentally Unfit: Detection, Elimination and Disposal.
Lieut. Col. Roy R. Grinker, Psychiatric Disorders in Combat Crews Overseas and in Returnees.
Dr. Edwin G. Zabriskie, New York, Nervous Disorders in the Armed Forces.
Capt. Winchell M. Craig, M. C., Injuries to the Central Nervous System.
Dr. Howard C. Naffziger, San Francisco, Injuries to the Peripheral Nervous System.
Luther E. Woodward, Ph.D., New York, Social Readjustment of Returning Veterans.
Lieut. Comdr. Howard P. Rome (MC), The War and Its Psychiatric Problems.
Dr. David J. Margolis, Chicago, Compensation Laws and the Veterans Administration.
Dr. Sidney I. Schwab, St. Louis, Residuals of Neuropsychiatric Disorders.
Dr. Ernest Sachs, St. Louis, Residuals of Neurosurgical Disorders.

The program will include a series of panel discussions on war neuroses or battle fatigue? war injuries to the nervous system, does war modify the behavior of the civilian population? and who are the mentally unfit for military service? The first evening session will include a neuropsychiatric "information please" program with Dr. Foster Kennedy, New York, as moderator. On the second evening Dr. Edward A. Strecker, Philadelphia, will deliver the seventeenth annual Pasteur lecture of the institute on "War Psychiatry and Its Influence on Postwar Psychiatry and Civilization."

KANSAS

Jack Austin Dies.—Capt. Jack F. Austin, executive secretary of the Sedgwick County Medical Society from 1937 until 1942, when he went into military service, was killed recently while on maneuvers in South Carolina, according to the *Medical Bulletin* of the Sedgwick County Medical Society.

William Abramson Named Supervising Ophthalmologist.—Dr. William F. Abramson, Topeka, has been appointed state supervising ophthalmologist for the division of service for the blind of the Kansas State Board of Social Welfare, succeeding Dr. William W. Reed, Topeka. The appointment is effective for an eighteen month period.

MASSACHUSETTS

Advisory Committee for Endorsement of Heavy Cream. — In Massachusetts authority has been given to the district supervisor of the Office of Distribution to make a reasonable interpretation of the terms of amendment 2 to War Food Order number 13, emanating from the Office of Distribution of the War Food Administration, providing that medical prescriptions for heavy cream must be approved by the public health officer or the secretary of the county medical society of the area where a patient or hospital is situated. The *New England Journal of Medicine* reports that the endorsing function has, by this interpretation, been vested in an advisory committee composed of John H. Sullivan, district

supervisor, Office of Distribution, War Food Administration, chairman; Dr. Vlado A. Getting, Boston, state commissioner of health; Dr. G. Lynde Gately, Boston, city health commissioner; Dr. H. Quimby Gallupe, Boston, secretary, state board of registration in medicine; Dr. Nathaniel W. Faxon, medical director, Massachusetts General Hospital, Boston, and Drs. Francis Gorham Brigham, Brookline; Joseph Garland, Boston; Loring Grimes, Swampscott, and Franklin W. White, Boston, representing the Massachusetts Medical Society.

MICHIGAN

Seminar on Speech Rehabilitation.—The speech clinic of the University of Michigan, Ann Arbor, announces an intensive training course for veterans with speech and hearing disabilities. The course will begin November 6 and continue for six weeks. This program will be similar to one mentioned in THE JOURNAL, June 17, page 504.

Personal.—Melville Sahyun, Ph.D., has been named divisional vice president of Frederick Stearns and Company, Detroit, Division of Sterling Drug, Inc. Dr. Sahyun has been associated with Stearns since 1934, first as director of biochemical research and since 1943 as director of research. He developed the first amino acid preparation for parenteral administration in man and his book "An Outline of the Amino Acids and Proteins" will soon be published.

Fredrick Yonkman Joins Ciba Company.—Dr. Fredrick F. Yonkman has resigned as professor of pharmacology and therapeutics and chairman of the department at Wayne University College of Medicine, Detroit, to accept a position as chief pharmacologist in the research division of Ciba Pharmaceuticals, Inc., of Summit, N. J. Other changes in the pharmacology staff include the resignation of Dr. Harold F. Chase, assistant professor, to accept a similar position in the Western Reserve University School of Medicine, Cleveland, and Bradford N. Craver, Ph.D., as research associate to become instructor and director of pharmacologic research conducted under governmental contract at the University of Rochester, N. Y.

NEW JERSEY

Personal.—Dr. Jacob Cohen, formerly acting clinical director of Central Islip State Hospital, Central Islip, N. Y., has been appointed assistant director of the Newark State School, Newark. Since the death of Dr. August E. Witzel, May 15, Dr. Hiram G. Hubbell, assistant director (superintendent), has been acting director.

Foremen Should Not Dispense Acetylsalicylic Acid.—Newspapers reported on August 12 that Dr. J. Lynn Mahaffey, Trenton, state director of health, made a recommendation to the Ford Motor Company at Edgewater that it discontinue a recently established practice of allowing foremen to dispense aspirin (acetylsalicylic acid) to workers complaining of minor ailments. It was stated that the health director also recommended that the company revert to its old procedure of allowing workers complaining of minor ailments to visit, on the company's time, first aid stations in the plant staffed with medical personnel.

Medical School to Open October 1.—The Essex College of Medicine, said to be the first institution of its kind in New Jersey, plans to open about October 1 in a three story building at Broad Street and Third Avenue, Newark, according to the New York *Times*. The facilities include an auditorium, twenty-five classrooms and laboratories. A prospective faculty of fifty members is available, it was stated. The state board of education recently ruled that the school might not issue the degree of doctor of medicine until it has been in existence two years. In a statement to the press, Samuel R. Herbster, registrar, is reported to have said "The board encouraged us to open on that basis. It's a testing period, a trial period that they wanted us to go through, and we'll open on that understanding." The registrar also stated that more than 200 applications, mainly from New Jersey residents, had been received, and that the institution would open as soon as 100 had been accepted. For the first four years only 100 students would be accepted each year, it was stated.

NEW YORK

Personal.—A surprise party was held for Dr. Christopher G. Parnall recently in celebration of his twentieth anniversary as medical director of the Rochester General Hospital, Rochester.

Physician Observes Ninety-Fifth Birthday.—Dr. Gerrit F. Blauvelt, Nyack, former president of the Rockland County Medical Society, observed his ninety-fifth birthday August 1. Dr. Blauvelt is the sole surviving incorporator of the Nyack Hospital.

Free X-Ray Service to Public.—The Ontario County Committee on Tuberculosis and Public Health plans to make available free roentgenograms of the chest to every one, newspapers reported. The plan is an expansion of the original one of limiting the service to industrial employees only. Tests will be made by a visiting mobile x-ray unit that will tour the county and will be available to any one wishing to do so.

Physicians Honored.—Dr. Festus M. Chaffee was given a dinner in the Middlesex Town Hall, August 1, for his forty years of service to the commnity.——The Wayne County Medical Society on August 8 gave a dinner in honor of four members who have completed fifty years in the practice of medicine. The physicians are Drs. George D. Winchell, Rose; Cyrus P. Jennings, Macedon; Samuel L. Houston, Wolcott, and Ralph Sheldon, Lyons.

Outbreak of Food Poisoning.—Ninety-two members of the staff at Strong Memorial Hospital, Rochester, became ill, August 17. Fifty-two were hospitalized and 40 others were unable to report for duty. An investigation disclosed that the outbreak was attributed to bacteria infected egg salad sandwiches which had been served to members of the staff. None had been served to the patients of the hospital. Among the persons ill were medical students, physicians and dietitians. The 40 less severe cases were among student nurses, who were treated at their homes, the Rochester *Times-Union* reported.

New York City

Louis Julianelle Dies.—Louis A. Julianelle, Ph.D., chief of the division of infectious diseases, Public Health Research Institute, died in Memorial Hospital for the Treatment of Cancer and Allied Diseases, August 12, aged 49. Dr. Julianelle received his Ph.D. at the University of Pennsylvania in 1922, subsequently serving there as instructor in bacteriology. After a number of years of service at the Hospital of the Rockefeller Institute, Dr. Julianelle joined the staff of Washington University School of Medicine, St. Louis, serving there from 1930 to 1942, when he went to New York.

The Lewis Cass Ledyard Fellowship.—Applications are now being accepted for the Lewis Cass Ledyard Jr. Fellowship by the Society of the New York Hospital. Three thousand dollars will be available as a stipend to an investigator in the fields of medicine and surgery or in any closely related field and about $1,000 for supplies or expenses of the research. Preference will be given to younger applicants who are graduates in medicine and who have demonstrated fitness to carry on original research of high order. Applications should be received by the Committee of the Lewis Cass Ledyard Jr. Fellowship not later than December 15. It is expected that the award will be made by March 15, 1945. Additional information may be obtained from Dr. Eugene F. Du Bois, chairman of the committee, Society of the New York Hospital, 525 East 68th Street. The fellowship was established in 1939 by a gift from Mrs. Ruth E. Ledyard in memory of her late husband, Lewis Cass Ledyard Jr., a governor of the New York Hospital.

Course in Industrial Medicine.—The Long Island College of Medicine, Brooklyn, will conduct its third postgraduate course in industrial medicine October 16 to November 3 under the auspices of the department of preventive medicine and community health. The course intends to provide physicians engaged in full time or part time industrial practice, as well as those who wish to enter this field an opportunity to orientate themselves more fully to modern procedures in the rapidly developing specialty of industrial medicine. This year the course will place particular emphasis on postwar conditions and problems associated with the return of workers from military service. Although designed for graduate physicians, the course will be open to industrial executives, personnel workers, industrial nurses, hygienists, engineers and others interested in industrial health. The course will include afternoon and evening lectures and seminars at the college supplemented by morning clinics and demonstrations arranged in cooperating hospitals and industrial medical departments. Sections of the course will be devoted to medical administration in industry, industrial aspects of internal medicine, industrial surgery, occupational diseases and personal relations in industry, with emphasis on the medical aspects of personnel problems. Additional information may be obtained from Dr. Thomas D. Dublin, 248 Baltic Street, Brooklyn 2.

OKLAHOMA

Narcotic Violation.—Dr. William T. Huddleston, Konawa, pleaded guilty in the U. S. District Court at Muskogee, June 28, of a violation of the federal narcotic laws. The physician was sentenced to pay a fine of $800 and was placed on probation for a period of five years.

The Leroy Long Memorial Lecture.—Dr. George M. Curtis, Columbus, Ohio, gave the Leroy Long Memorial Lecture in Oklahoma City, June 21, on "Surgery of the Spleen." The lecture is sponsored by the alumni and undergraduates of Phi Beta Pi as a memorial to the late Dr. Leroy Long, Oklahoma City, dean of the medical school from 1915 to 1931.

Annual Conference.—The Oklahoma City Clinical Society will hold its fourteenth annual clinical conference at the Biltmore Hotel, Oklahoma City, October 23-26. Among the speakers will be:

Dr. Nathaniel G. Alcock, Iowa City, urology.
Dr. O. Theron Clagett, Rochester, Minn., surgery.
Dr. Charles C. Dennie, Kansas City, Mo., dermatology.
Dr. Lawrence P. Engel, Kansas City, surgery.
Dr. George P. Guibor, Chicago, ophthalmology.
Dr. Tinsley R. Harrison, Dallas, Texas, medicine.
Dr. Harold O. Jones, Chicago, gynecology.
Dr. Ralph A. Kinsella, St. Louis, medicine.
Dr. Hugh McCulloch, St. Louis, pediatrics.
Dr. Ralph H. Major, Kansas City, medicine.
Dr. William F. Mengert, Dallas, obstetrics.
Dr. Alan R. Moritz, Boston, pathology.
Dr. Henry H. Ritter, New York, surgery.
Dr. George E. Shambaugh, Chicago, otolaryngology.
Dr. James S. Speed, Memphis, Tenn., orthopedic surgery.
Dr. Bruce K. Wiseman, Columbus, Ohio, medicine.
Dr. Herman L. Kretschmer, Chicago, President, American Medical Association.

PENNSYLVANIA

Foreign Nonprofit Organizations and Medical Service.—The Department of Justice of Pennsylvania has ruled that foreign nonprofit corporations cannot enter the state to provide or render medical services to individuals except when specifically authorized by statute, according to *Philadelphia Medicine.*

Schireson Obtains Injunction Against State Board.—A temporary injunction was recently issued by the Dauphin County Court restraining the state board of medical education and licensure from conducting a hearing on a citation against Dr. Henry J. Schireson, Philadelphia, to show cause why his license should not be revoked. The hearing was to have been held July 14.

RHODE ISLAND

Personal.—Paul J. Spencer of Butler Hospital, Providence, has been appointed secretary of the New England Hospital Assembly to succeed Gerhard Hartman, director of Newton Hospital, Newton, Mass., resigned.

Butler Hospital Observes Centennial.—Butler Hospital, Providence, will hold its second and final observance of its one hundredth anniversary on October 4. The program is intended to interest the lay public, and a special evening session will be held at the Rhode Island School of Design. Governor J. Howard McGrath is expected to attend the meeting. Other speakers will include:

Dr. Elihu S. Wing, Providence, president, state medical society, a message from the medical profession.
Clemens J. France, director, Rhode Island State Department of Social Welfare, an appreciation from social welfare.
Col. H. Edmund Bullis, A Hundred Years of Service in Mental Health.
Dr. Arthur H. Ruggles, superintendent, Providence, A Few Remarks on the Past, the Present and the Future of Rhode Island's Oldest Hospital.

GENERAL

Physician Needed in West Africa.—Dr. George W. Harley, who recently returned to this country because of an emergency health condition, announces that a physician is urgently needed in Ganta, Liberia, West Africa. The emergency was created when Dr. Harley, founder of the Ganta Mission, was compelled to return to the United States. The area to be served is inhabited by more than a million natives and 25 or 30 white missionaries. Physicians in contingent mission stations have gone one by one to join the Unted States armed forces. At the dispensary handled by Dr. Harley the work is now carried on with the aid of a school teacher, Miss Mildred Black, who is not even a nurse, and a couple of schoolboys who help in the treatment of about 200 patients with leprosy and assist with intramuscular and intravenous injections each week. These injections are mostly for yaws, trypanosomiasis, schistosomiasis and other skin diseases. The position is available to a doctor of medicine who has graduated at an approved medical school and who has had two years' internship or residency. The salary is moderate, with allowances for wife and children; travel expenses will be paid. A communication from Dr. Harley indicates that the position offers experience in tropical medicine and includes facilities for research in trypanosomiasis and leprosy.

Accident Facts.—The National Safety Council has just brought out its 1944 edition of "Accident Facts," which presents a comprehensive report on accidents of all types. The booklet states that the 1943 accidental death toll was 97,500, an increase of about 2 per cent over 1942. Accidental injuries in 1943 totaled about 10,100,000, about 350,000 of which resulted in some permanent disability ranging from a finger amputation to permanent crippling. Accident costs totaled approximately $4,900,000,000, including wage loss, medical expense, overhead costs of insurance, property damage in motor vehicle accidents and fires, and the so-called indirect costs of occupational accidents. Motor vehicle accidents accounted for 23,400, a 17 per cent decrease from 1942. Public nonmotor vehicle accidental deaths of civilians totaled 17,000, a 6 per cent increase over the previous year. There were 32,500 civilian home accident fatalities in 1943, an increase of 7 per cent over 1942. Deaths of civilians in occupational accidents totaled 18,000, or 3 per cent less than in 1942. Accidental deaths of military personnel in the United States accounted for 11,500 deaths, a 69 per cent increase over 1942. The most important single type of accidental death in 1943 was falls, replacing motor vehicle accidents, which had for twenty years resulted in the largest annual death total. Falls accounted for 27,400 deaths, giving a rate per hundred thousand of 20.3, an increase of 7 per cent over 1942. The total increase since 1933 amounted to 17 per cent.

American Hospital Meeting.—The annual convention of the American Hospital Association will be held at the Hotel Statler and Public Auditorium, Cleveland, October 2-6. The preliminary program includes the following speakers:

Thomas S. Gates, LL.D., President, University of Pennsylvania, Philadelphia, The Commission on Hospital Care.
Dr. Arthur C. Bachmeyer, director, University of Chicago Clinics, Hospital Trends.
Dr. Morris Fishbein, Editor, THE JOURNAL, The Physician and Public Health.
Dr. Julius L. Wilson, New Orleans, Tuberculosis, the Hospital and Public Health.
Dr. John R. McGibony, Washington, D. C., Program of the Indian Service Hospitals.
Dr. Edwin Dwight Barnett, Santa Rosa, Calif., Hospital and Public Health Under One Administration.
Dr. Ephraim M. Bluestone, New York, Basic Principles of Medical Social Work.
Dr. Herman G. Weiskotten, Syracuse, N. Y., Medical Care of the Discharged Hospital Patient.
Dr. Cassius H. Watson, New York, Trends in Outpatient Service.
Dr. Harold M. Coon, Madison, Wis., Hospitals' and Nurses' Personnel Relations.
Dr. Clarence H. Bellinger, Brooklyn, Organization and Management of Shock Therapy Service.
Dr. Melbourne G. Westmoreland, Council on Medical Education and Hospitals, American Medical Association, Where is the Record Librarian Coming From?
Dr. Victor Johnson, Secretary, Council on Medical Education and Hospitals, American Medical Association, What Should the Returning Doctor Expect from His Hospital?
Col. Richard P. Strong, M. C., Our Hospitals' Problems in Diagnosing and Treating Tropical Diseases.

International College of Surgeons.—The ninth national assembly of the United States chapter of the International College of Surgeons will be held at the Benjamin Franklin Hotel, Philadelphia, October 3-5, under the presidency of Dr. Thomas A. Shallow, who will speak on "Radical Treatment of Carcinoma of the Esophagus." Included among the speakers will be:

Dr. George M. Piersol, Philadelphia, Rehabilitation.
Dr. Desiderio A. Roman, Philadelphia, The Classic Cesarean Section, with Analyses of 53 Cases Operated on by the Author.
Dr. Leonard Averett, Philadelphia, Vaginal Hysterectomy: Indication and Advantages.
Dr. Frances I. Seymour, New York, The Responsibility of the Surgeon in the Preservation of Human Fertility.
Dr. Roy W. Mohler, Philadelphia, An Analysis of the Indications, Results and Dangers of Complete and Supravaginal Hysterectomy.
Dr. Clifford B. Lull, Philadelphia, Caudal Analgesia.
Dr. Karl F. Schlaepfer, Milwaukee, Pentothal Sodium Anesthesia in Major Surgery and Its Dangers.
Dr. Charles M. Griffith, Washington, D. C., The Rehabilitation of Ex-Members of the Armed Forces by the Veterans Administration.
Capt. Howard H. Montgomery (MC), Rehabilitation in the Navy.
Major General George F. Lull, M. C. (subject not announced).
Vice Admiral Ross T. McIntire, Surgeon General of the Navy (subject not announced).
Dr. Thomas B. Noble Jr., Indianapolis, The Surgical Control of Obstructive Adhesions of the Small Bowel.
Dr. John E. Cannaday, Charleston, W. Va., The Cutis (Derma) Graft Transplant.
Dr. Robert H. Ivy, Philadelphia, Principles of Skin Graft.
Dr. Lyman Weeks Crossman, New York, Refrigeration for the Preservation of Traumatized Tissue.
Dr. John Royal Moore, Philadelphia, Massive Bone Defects.
Dr. Custis Lee Hall, Washington, D. C., Osteotomy for the Treatment of Ununited Fractures of the Femoral Neck.

Dr. Austin T. Moore, Columbia, S. C., Fractures of the Hip Joint: Treatment with Adjustable Nails or Blade Plate Fixation.
Dr. Roger Anderson, Seattle (subject not announced).
Drs. Harry E. Bacon, Orville C. Gass and William D. Todhunter, Philadelphia, Cancer of the Rectum and Pelvic Colon, with Special Reference to Preoperative and Postoperative Treatment.
Dr. William Seaman Bainbridge, New York, A Survey of Surgical Results in Cancer.
Dr. Albert A. Berg, New York, The Preservation of the Sphincter Ani in Radical Operation for Cancer of the Rectum.
Dr. Elmer Hess, Erie, Pa., The Indications for Transplantation of the Ureters, with a New Surgical Technic.
Dr. Oswald Swinney Lowsley, New York, Plastic Operations on the Kidneys.
Dr. Rudolf Nissen, New York, A New Technic of Operation for Cysts of the Lung and for Chronic Spontaneous Pneumothorax.
Dr. Frederick M. Allen, New York, Surgical Shock and Its Treatment.
Dr. Richard H. Lawler, Chicago, Gastric Surgery.
Dr. Sebastian J. Carnazzo, Omaha, Subtotal Gastric Resection for Peptic Ulcer.
Dr. Max Thorek, Chicago, History and Practical Application of Tubovalvular Gastrostomy.
Dr. Moses Behrend, Philadelphia, Ulcerative Leiomyoma of the Stomach.
Dr. Asher Winkelstein, New York, The Relation of Gastric Acidity to Recurrent Ulcers After Partial Gastrectomy.
Dr. Otto De Muth, Vancouver, B. C., Recent Developments of Biliary Surgery.
Nicholas A. Michels, D.Sc., Philadelphia, Variations in the Arterial Blood Supply of the Liver, Gallbladder, Stomach, Duodenum and Pancreas.
Robert Lich Jr. and Ralph B. Samson, U. S. Public Health Service Reserve, A Method of Inguinal Herniorrhaphy.
Miss Helen S. Willard, director, Philadelphia School of Occupational Therapy, Occupational Therapy in Rehabilitation.
Dr. William A. Lell, Philadelphia, Observation on the Bronchoscopic Insufflation of the Sulfonamides into the Tracheobronchial Tree.
Dr. Benjamin I. Golden, Elkins, W. Va., Massive Single Doses of the Sulfa Drugs.
Dr. Elias D. Lawrence, Paterson, N. J., Saphenous Vein Ligation.
Dr. Edmund B. Spaeth, Philadelphia, Aneurysm of Circle of Willis from an Ophthalmological Standpoint.
Dr. Samuel R. Skillern, Philadelphia, The Frontal Sinuses as the Pathway of Infection to the Cranium and Its Contents.
Dr. Ben Robnett Dysart, Pasadena, Calif., Diabetic Gangrene Involving the Sinuses.

The program will include a series of round table discussions and scientific and technical exhibits and motion pictures. On Wednesday evening the convocation address will be delivered by Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, on "The Organization of American Medicine." The assembly dinner will be held Thursday evening.

FOREIGN

Dr. Aldo Castellani Reported Suspended from Rome Faculty.—Dr. Aldo Castellani, who formerly served as professor of tropical medicine at Tulane University of Louisiana School of Medicine and Louisiana State University Medical Center, New Orleans, is reported to be one of twenty-five members of the faculty of the University of Rome who have been suspended. According to *Science*, the *Times*, London, states that the majority of these men had either been ministers in the fascist government or had held high appointments in the corporations.

Special Lectures.—At the recent sixth annual meeting of the Royal Australasian College of Physicians, Sydney, Australia, a portrait of the first president of the college, Sir Charles Bickerton Blackburn, was unveiled. Special lectures delivered as a part of the meeting included the second G. E. Rennie Memorial Lecture by Sir C. Trent Champion de Crespigny, London, on "Torula Infection of the Central Nervous System" and the second Annie B. Cunning Lecture by Dr. C. G. McDonald on "Diet and Disease." Other speakers included Lieut. Col. J. Erskine Sewell on "Notes on Scrub Typhus from the Observation of 500 Cases," Dr. T. M. Greenaway, "Hyperinsulinism Due to Pancreatic Adenoma" and Dr. S. V. Sewell, "The Results of Sympathectomy in the Treatment of Severe Cardiac Pain, Headache and So Forth."——Dr. Thomas L. Hardy recently delivered the Croonian Lectures before the Royal College of Physicians of London on "Order and Disorder in the Large Intestine."

Report Dr. Carrel Ousted.—On August 28 the Associated Press reported that Dr. Alexis Carrel, emeritus member of the Rockefeller Institute for Medical Research, New York, and associate member of the American Medical Association, had been dismissed from his position as director of the Vichy government's Foundation for the Study of Human Relations. The information was said to be broadcast over the Paris radio and further intimated that the foundation had been "notorious for its actions detrimental to the French nation." Dr. Carrel, who is 71 years of age, is a native Frenchman who retained his citizenship despite many years spent in the United States. A newspaper report on August 30 indicated that Dr. Carrel had been arrested by the French Forces of the Interior on charges that he had "founded his institute with Vichy support for the purpose of supplanting the great French universities, and introducing fascism and Marxism to the students." It was further stated that the Petain régime donated funds freely to Dr. Carrel's institute, the initial gift amounting to about $800,000, with the intention of hiring away professors from the Sorbonne and other universities. It was further alleged that Dr. Carrel tried to close university laboratories so that professors would have to come to his institute to earn their living.

Government Services

Charles Williams to Direct States Services

Dr. Charles L. Williams, who has been stationed in New Orleans as medical and district director for the U. S. Public Health Service district number 4 since July 1, 1940, was to have been transferred on August 16 to Washington, D. C., as assistant surgeon general. He will be in charge of the Bureau of States Services (THE JOURNAL, Dec. 11, 1943, p. 983) and will be promoted to the rank of brigadier general.

Private Home Given to Public Health Service

Hilhome in Westchester County, New York, estate of the late Percy S. Straus, became on August 11 the property of the U. S. Public Health Service, which will make it a convalescent home for merchant seamen and Coast Guardsmen. The presentation of the deed by Mrs. Straus was made in a special ceremony in the headquarters of the U. S. Public Health Service in Washington, D. C. In accepting the deed Dr. Thomas Parran, Surgeon General, U. S. Public Health Service, is reported to have said that the home may be converted into a convalescent home with 75 beds and, subject to Presidential approval, will be the site of a permanent hospital under the postwar program of the public health service. The property includes a 112 acre tract partly in the town of Rye and partly in the town of Harrison and is located 4 miles north of Port Chester. Hilhome will be available for hospital use immediately and will be adapted for permanent hospital service. During the twenty-five years that it has been the home of the Straus family, more than a million dollars has been expended on the property above the original cost. Mr. Straus was formerly chairman of the board of R. H. Macy and Company.

Funds for Public Works

The President, July 10, approved allotment of federal funds totaling $1,412,488 for thirty war public works and services projects in seventeen states, including hospital and child care facilities and schools in war impacted communities, Major General Philip B. Fleming, federal works administrator, announced. A grant of $291,802 will match funds of the Sisters of St. Francis for constructing and equipping a 100 bed hospital in Detroit to cost an estimated $583,604. A second grant in the Detroit area is for $30,800 for an addition to the Burton School in Royal Oak Township. Federal contributions of $222,324 and $199,886 go to the U. S. Public Health Service for continued assistance in the maintenance and operation of venereal disease hospital facilities in Chatham County and in Augusta, Ga., respectively. More than 2,100 patients have been treated in these centers. A grant of $75,700 was made to the Allegany Hospital of the Sisters of Charity in Cumberland, Md., providing for the dismantling and transporting of a demountable dormitory from Dublin, Va., and constructing, altering and equipping the building to provide training facilities for student nurses. A grant of $34,500 will match an equal amount provided by the Medical College of Virginia, Richmond, for remodeling a part of St. Philip Hospital in Richmond, to expand training facilities for 185 student nurses. Six California communities will receive funds for child care centers and for school maintenance. Other projects were approved in Alabama, Arizona, Idaho, Missouri, Oregon, North and South Carolina, Pennsylvania and Texas.

CORRECTION

Officers of Pathology Board.—The name of Major R. Philip Custer, M. C., was inadvertently omitted from the news item carrying the names of new officers of the American Board of Pathology (THE JOURNAL, August 12, p. 1051). Major Custer was chosen trustee-at-large of the board.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 5, 1944.

The Rebuilding of Guy's Hospital

Guy's Hospital is known all over the world not only as a great teaching center but also for the advances in English medicine emanating from it. The clinician Jonathan Hutchinson once said "Diseases seem to have been made in order that Guy's physicians should discover them." No doubt he had in mind the eponymous diseases of Bright, Addison and Hodgkin, who were elder contemporaries of his. This famous hospital has been badly damaged by German bombs, but arrangements have already been made, thanks to the munificence of Lord Nuffield, to restore it with every modern equipment and to build a new college for students. The eighteenth century buildings, which have survived and are suitable for modern requirements, will be combined with new buildings. Now located in the country (whither bombing has made many of the London hospitals resort) is what is known as "Guy's U. S. A. Hospital," because it was started as a wartime measure largely by American help. It is thought that this should prove of great value in working out the bigger plan for a permanent country Guy's. Planning is not restricted to building. A closer fusion of the hospital with its medical and dental schools into a great teaching center is contemplated. Already new fields are opening up. A recent development, the York Clinic for Psychoneuroses, is the only one of the kind in the country associated with a teaching hospital. Guy's has the largest dental school, and it is hoped that arrangements can be made for every patient to receive not only expert dental treatment but also any other treatment necessary. It is also proposed to establish a university chair in dental medicine and to make a study of the relations between dental disease and disease processes in general.

Labeling of Foods to Protect the Public

The Ministry of Food has issued an order on food labeling which is intended to ensure wholesome quality and to make certain that the public gets what it expects. Under the new ruling, certain requirements must be met by the labels of all prepacked foods (those packed or made ready in advance for retail sale in a wrapper or container). The labels must show the name and address or registered trade mark of the person for whom the food is packed and the name or usual name of the food. Foods containing more than one ingredient must show the usual name of the ingredients in the order of the proportions in which they were used and the minimum quantity of food in the package. Foods claiming to contain vitamins or minerals are subject to special rules. Claims must not be made on the labels or in advertisements unless supported by a statement of the nature of the vitamin or mineral present and the quantity. Fruit and vegetables are exempt from this order unless canned or boiled.

The Accidental Discovery of Penicillin

In an address at the King's Chapel of the Savoy on Hospital Sunday (when donations for the hospitals are collected), Alexander Fleming, the discoverer of penicillin, delivered an address. The discovery, he said, illustrated the great value of the freedom to pursue research which was so prominent in the voluntary hospital and might be restricted under a more bureaucratic system. Like many bacteriologists, Professor Fleming related, he had many culture plates contaminated with mold spores which drop from the air, and, like every other bacteriologist, he had cast them out with suitable expressions of annoyance. But on this one occasion he did not, and penicillin was the result. He noticed that the molds prevented growth of the culture for a small area. It seemed providential that the most powerful agent against septic infection was discovered at this time, when we were plunged into a bloody war. Penicillin has already done much to alleviate the sufferings of the wounded, Fleming stated, and will do more as the supply increases. In the last war the infected wounds of many soldiers remained open for six months or more, with frequent painful dressings. Now it is hoped that by the aid of penicillin they will not become infected at all or that, if they do, many will heal in a month or less.

The Site for Intramuscular Injections

In the correspondence columns of the *British Medical Journal* attention is called to the danger of using the gluteal muscles as a site for intramuscular injections. This practice is not only in vogue but is taught in our leading hospitals, it is stated by Prof. Grey Turner, who recalls that he pointed out its dangers as long ago as 1920. After the first world war he observed that several soldiers were victims of severe and persistent neuritis or paralysis of the great sciatic nerve as a result of injecting quinine solutions into the nerve instead of into the mass of the gluteal muscle. A case of death from sloughing also came to his knowledge. After the malaria epidemic in Ceylon there were at least 2 cases of severe secondary hemorrhage from the superior gluteal artery complicating abscess due to injecting quinine into the buttock. In 1941 A. W. Frankland stated in the *Journal* that if solutions of sulfapyridine are administered deeply into the gluteal region there is grave danger of injury to the larger branches of the sciatic nerve. He quoted 6 cases of foot drop with varying degrees of anesthesia, and also cases of gluteal paresis. Recently one of the larger provincial hospitals was forced to pay damages of several hundred pounds because a patient developed sciatic paralysis after an injection in the gluteal region.

Professor Turner again urges that the outer side of the thigh is the proper place for such injections. The vastus externus is a large muscle, is protected by the fascia lata and is not traversed by any important vessels or nerves. The muscular mass is of large capacity and as much as 500 cc. can be introduced into its substance, provided the injection is done slowly. The technic is simple, Professor Turner claims. A point on the middle of the outer side of the thigh is selected, and the hollow needle is thrust at right angles to the surface. It is enough to insert it just beneath the fascia lata—a point which can readily be determined by the sensation of yielding resistance after penetration or by introducing the needle to the average depth of about an inch. If the needle strikes the bone no harm is done, provided it is withdrawn about half an inch before injecting. If necessary, injections of small bulk may be made repeatedly in this situation. It is reasonable to vary the area of injection by starting near the top of the thigh and working down to about 3 inches above the knee; or the outer side of the other thigh may be used alternately. Injection of a particularly irritating solution or introduction of infection may result in abscess, but that is about the worst that can happen. The risk of phlebitis and generalized systemic infection associated with rigors is eliminated, Professor Turner says.

The *Army Medical Department Bulletin* also deals with the subject of intramuscular injection, particularly in battle casualties. The *Bulletin* points out that the injection should be made into healthy muscle. The gluteal muscles are perhaps most often chosen. They are extensive enough to absorb a good volume of fluid. It is important to keep clear of the sciatic nerve and related vessels. The upper and outer quadrant alone may be regarded as a suitable area for injection; it has a good thickness of muscle, lies well away from the sciatic nerve and is not pressed on as the patient lies in bed. Many other muscle groups are suitable. It is unnecessary to put a badly wounded

man to the discomfort of turning him on a stretcher simply to give an intramuscular injection into his buttock, the *Bulletin* states. The external thigh muscles, deltoid muscle and pectoral muscles are often more conveniently accessible. Indeed, any large muscle away from important vessels or nerves may be used.

AUSTRALIA

(From Our Regular Correspondent)

May 20, 1944.

Problems of Anthropology in the Pacific

While the war is still raging in the Pacific it may seem premature to consider proposals for the future government and development of native races in the South Pacific islands. Yet, assuming that Australia's interest and responsibility in relation to mandated territories will be retained and possibly extended when the war is over, it is obvious that the welfare of the territory natives, whose friendship and assistance in the present conflict are of inestimable value to the Allied nations, must be taken into account in planning for postwar reconstruction.

This question is raised by J. W. Burton in a pamphlet entitled "Brown and White in the South Pacific," published by the Australian Institute of International Affairs. He declares that the impact of the present catastrophic war will affect the life and social order of the native races to an extent which at this stage cannot be determined, but it is obvious that the results will be deep and far reaching.

When Australians read of the heroic and unselfish part taken by the native stretcher bearers of Papua and New Guinea in the campaign against the Japanese, few give a thought to the effects of the war on social life of the island natives, the disruption caused in homes and villages, the demoralizing effect on the younger natives, the problem of restoring native agriculture and normal conditions of community life when peace returns.

Burton's pamphlet deals first with the native culture in the Pacific—a very old culture with roots that go deep into the past. "One may live for weeks in a native village," he says, "and feel its rhythm and charm, enjoy its laughter and gaiety, watch its colorful ceremonies and yet not suspect that the simplest actions and most commonplace habits have a long ancestry behind them and that every part of the common life is regulated by almost imperceptible rules of conduct." He states too that the South Sea social organization has been classed by some as communistic, although not in any marxian sense, and this element is admittedly present, for the life of the village is assuredly based, perhaps quite unconsciously, on the principle of "each for all and all for each." In Fiji, for instance, all land is held by the mataqali, or clan, and can never be alienated unless the mataqali itself dies out. While every man has his own house (in Fiji usually of an excellent type), no one can sell his house to another. Like the land, it belongs to the people as a whole, and the occupant has only the use of it.

It is pointed out that under this system there was no danger of property falling into a few hands, as with us. Mutual ownership of property prevented accretions of wealth and thereby restricted temporal power. No man ever went hungry, except for some visitation of nature, such as drought or flood; no one went unemployed, although there was abundant leisure.

With the introduction of the plantation system by white men came the indenture of native labor. It is true, says Mr. Burton, that the indenture system has its good side as far as the native is concerned. On the other hand, from the moral point of view, life on the plantations is far from ideal. Large numbers of men, separated for years from their womenfolk and from the healthy influence of children, contract vices such as gambling, thieving and general irresponsibility, and return to exercise a bad influence on the village.

As to the evidence of the effects of the present war on the native life and social order, Mr. Burton says "In areas, particularly in the southeastern Pacific, where the actual devastation of war has not been felt, there are serious repercussions. The presence of tens of thousands of European servicemen, with plenty of money to spend and abundant leisure, has had a profound and immediate effect on native economy. There has come such an abundance of wealth that it has resulted in many places in natives neglecting their gardens and villages; they are content to do a little washing for the troops or sell a few curios at ridiculous prices and then spend their money in buying tinned meats and preserved fruits from the trader's store."

There is too, Mr. Burton adds, a serious disregard for the village authority, and the young girls have had their heads turned by the attentions of random admirers while their own men are away at other theaters of war. "There is no vivid imagination required to sense the dangers here," he says. "The case of those islands, particularly the Solomons, Papua and New Guinea, where the ravages of war have been so terrible, is even worse. No estimate can be made of the physical damage done. Hundreds of people have been killed, thousands have been torn away from their villages, and, although they have won a great name as stretcher bearers and carriers, no one may estimate the rupture of the social fabric of their lives."

There is evidence that both United States and Australian armies are conscious of these problems and are taking action to overcome them.

Australian Reaction to British Criticism of Medical Students' Training

The report of the planning committee of the Royal College of Physicians aroused interest here. The report stated that the average medical graduate has defects chiefly attributable to the manner of his training. He tends to lack curiosity and initiative. His powers of observation are relatively undeveloped, his ability to arrange and interpret facts is poor and he lacks precision in the use of words. In short, his training, however satisfactory it may have been in the technical sense, has been unsatisfactory as education.

Increase of scholarships as a method of overcoming financial barriers to the profession has the defect of compelling a boy to specialize in order to pass examination, at the expense of general education, especially in activities that develop personality and character. University education should be absolutely free, not only in medicine but in all other subjects. Allocation to universities would be on the merit of character plus ability, instead of wealth. Methods whereby the medical course itself can be improved include curtailment of certain traditional subjects, such as botany and topographic anatomy and, preeminently, division of medical education into two categories—the undergraduate course, which shall be general and unspecialized and designed to provide for doctors as a whole, and the postgraduate course, catering to special needs of gynecology, x-rays and other highly technical branches.

Dr. B. T. Zwar, deputy chancellor of Melbourne University and president of the Royal Melbourne Hospital, said that experience in the last war had shown that graduates of Australian medical schools compared very favorably with those from English schools, while our graduates who went to England were very highly regarded there. Dr. Swar said he agreed, however, that there was insufficient preliminary general education before university courses were begun. Up to this year Melbourne University had accepted students at 16 years of age; now it is 17, but he felt that was still rather young. In England the General Medical Council had laid down that no medical student could register until within three months of his eighteenth birthday. Dr. Zwar was particularly

glad to note that the planning committee of the Royal College of Physicians had said that allocation to universities should be on "the merit of character, plus ability, instead of wealth." He said he had always advocated that some regard should be paid to the character of a student entering a profession; that was done in various American university medical schools, and the system had worked quite satisfactorily.

BRAZIL

(From Our Regular Correspondent)

SÃO PAULO, July 22, 1944.

Treatment of Chronic Osteomyelitis with Penicillin and Surgery

At the last meeting of the National Academy of Medicine a paper was presented by Dr. Mauricio Gudin on the treatment of 2 cases of chronic osteomyelitis in which surgery, under conditions of "integral asepsis of the environment," was associated with the use of penicillin. Dr. Gudin constructed, several years ago, a closed and entirely aseptic operating room, which he uses for his daily work at the Benificencia Portugueza Hospital of Rio de Janeiro. This whole aseptic operating technic has also been adopted by a few surgeons of Paris, where the system was considered worth while. In Dr. Gudin's first case the illness began thirteen years earlier, and eight operations had been performed. Recently the patient had been treated, without result, with twenty-five intramuscular injections of penicillin prepared at the Oswaldo Cruz Institute. After the operation in the integrally aseptic room the patient received several local, intramuscular and intra-arterial injections of the same penicillin. The wound healed completely in seven days. The second patient became ill in 1937 and had been operated on three times by another surgeon. Dr. Gudin operated once more, this time under conditions of integral asepsis, and the wound was maintained opened. On the seventh day the dressing was undone in the aseptic room and it was ascertained that the wound was in good condition. On the fourteenth day the wound was again examined and a secondary suture was done. On the twenty-first day healing was judged complete. The treatment by penicillin was the same as in the first case.

Iodized Table Salt to Combat Goiter

Central Brazil has a great area where goiter is endemic, and iodine deficiency in several parts of this area has been ascertained. In order to help correct this situation Mr. João Alberto, coordinator of economic mobilization, signed a special order with the following main provisions: 1. All table salt to be consumed in the areas recognized as deficient in iodine shall be industrially processed to contain the amount of iodine judged appropriate by the Division of Food of the Office of the Coordinator. 2. The product to be immediately sold under the name of "iodized table salt" shall contain 10 mg. (15 grains) of iodine per kilogram (2.2 pounds) of table salt. 3. The Division of Food will furnish technical assistance to table salt producers to insure the effectiveness of this order. The order also established a limit on the increase in price to be charged for iodized table salt.

Relief of Pain in Renal Colic

Prof. Luis Surraco and Dr. Lockart have presented a new treatment for renal colic. According to their recent publication in Montevideo they proposed the inhalation of amyl nitrite as an unproved means to relieve the pain.

The pain in renal colic arises from a spasm of the smooth muscular fibers, surrounding the ureter as well as the visceral ducts, and provokes regional contracture, to which there is added a ureteral distention above and a zone of ischemia below, the whole acting through appropriate stimuli on a special state of hyperreflectivity of the aortic-renal plexus.

It is understood that the therapy in crisis, in order to be useful, should take the form of a sedative for the hypersensitivity, an antispasmodic for the hypertonicity, a vasodilator favoring arterial irrigation and venous depletion. Responding to these demands, Surraco and Lockart have employed amyl nitrite, which has a well known action against the cardio-arterial spasm and which in renal colic produces the triple vasodilator, hypotensive and analgesic action through total intervention of the splanchnic nerves.

Immediately following inhalation they observed, together with the usual vascular phenomena, a complete and lasting cessation of the spontaneous pain, disappearance of the contracture of the abdominal wall through concomitant action on the striated muscular fiber and frequently a stimulation of diuresis. This quick action of the medicament is an important help in diagnosis in doubtful syndromes.

The immediate action of the amyl nitrite may be maintained and prolonged by employing glyceryl trinitrate after a few hours, repeating it according to the circumstances in the course of the first twenty-four or forty-eight hours.

Brief Items

Since the beginning of the war and the shortage of some medicinal products, the culture of Mentha piperita and the extraction of peppermint oil are being developed in São Paulo, Paraná and the other southern states of Brazil. At the price of $30 per kilogram of crystallized menthol, as set by the United States government for the importation of the drug, the production of menthol is one of the best paid extractive industries. A free booklet on the culture of the plant is being distributed by the division of information of the Department of Agriculture.

Ten years ago on June 6, Dr. Miguel Couto, professor emeritus of medicine at the University of Rio de Janeiro, died at the age of 72. Dr. Couto had a large private practice in Rio de Janeiro and has been considered by some the greatest Brazilian doctor of the present century. The Brazilian Academy of Medicine held a special meeting to commemorate this anniversary.

The National University of Rio de Janeiro is a semiautonomous organization financially supported in large part by the federal government. The government has recently bought a large plot of land known as the Valqueire Park in a northern suburb of Rio de Janeiro, in which will be constructed the new buildings of the university.

Dr. Augusto Paulino Jr. has been elected a member of the National Academy of Medicine. Dr. Paulino is professor of surgeory at the University of Rio de Janeiro.

The Brazilian Society of Ophthalmology recently held a meeting in which papers on endocrinologic problems in ophthalmology, tumors and refractive changes in diabetes were discussed. The most important papers were presented by Dr. Evaldo Campos, Dr. Orlando Cyrino and Dr. Sylvio de Campos.

Marriages

WILL BYRN ALSUP JR., Dublin, Ga., to Miss Martha Ham McRae of Charlotte, N. C., in Colorado Springs, Colo., August 4.

SAMUEL RICHARD STAGGERS, West Point, Miss., to Miss Sophy Malone Tilley of Durham, N. C., August 12.

JOHN JAY OSBORN, Garrison-on-Hudson, N. Y., to Miss Anne Mary M. Kidder of New York, August 6.

JAY EDWIN STOECKEL, Scranton, Pa., to DR. CATHERINE M. ROTH of Roanoke, Va., July 22.

GRAHAM BURT BLAINE JR. to Miss Patricia Smallwood, both of New York, August 5.

HENRY T. SIMMONDS to Mrs. Edythe Graeber Wetzel, both of Shamokin, Pa., July 28.

ROBERT L. DILTS, Fort Wayne, Ind., to Miss Virginia Lewis of Indianapolis, July 28.

JOHN T. MANNING, Muskegon, Mich., to Miss Betty E. Letts of Flint, July 29.

Deaths

Charles Hartwell Cocke ✠ Asheville, N. C.; Cornell University Medical College, New York, 1905; served an internship in the Presbyterian Hospital, New York, in 1906-1907; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians, serving once as chairman of the board of governors and vice president in 1942, 1943 and 1944; in 1926 vice president of the Medical Society of the State of North Carolina; past president and secretary of the Buncombe County Medical Society; in 1932 vice president of the Southern Medical Association and in 1937 chairman of its section on medicine; fellow and former vice president of the American College of Chest Physicians; member and in 1934 vice president of the American Clinical and Climatological Association; member of the American Trudeau Society, American Association of the History of Medicine, American Sanatorium Association, Southern Interurban Clinical Club and the National Tuberculosis Association; corresponding member of the International Union Against Tuberculosis; attending physician, Asheville Mission Hospital and the Biltmore (N. C.) Hospital; consulting physician to the Patton Memorial Hospital, Hendersonville; one of the medical directors and attending physician, Zephyr Hill Sanatorium; member of the chamber of commerce; served as secretary and heart and lung consultant to the medical advisory board during World War I; died August 3, aged 62, of coronary occlusion.

Frederick Brown Moorehead ✠ Chicago; Rush Medical College, Chicago, 1906; professor of oral surgery and head of the department of oral and plastic surgery and oral pathology at the University of Illinois College of Dentistry; formerly associate clinical professor of surgery (oral and dental) at his alma mater; chairman of the Section on Stomatology, American Medical Association, 1914-1915, 1915-1916; member and in 1926-1927 president of the American Association of Oral and Plastic Surgeons; member of the Institute of Medicine of Chicago, Chicago Pathological Society and the Chicago Historical Society; fellow of the American College of Surgeons; specialist certified by the American Board of Plastic Surgery; joint author of "Pathology of the Mouth"; consulting plastic surgeon, Illinois Central Railroad System; consulting oral and plastic surgeon, Home for Destitute and Crippled Children; attending oral and plastic surgeon, Presbyterian Hospital, where he died August 29, aged 68, of peritonitis due to perforated gastric ulcer and bronchopneumonia.

Herman Elwyn Pearse, Bonner Springs, Kan.; St. Louis College of Physicians and Surgeons, 1888; honorary member of the Kansas Medical Society; past president of the Missouri State Medical Association and the Jackson County (Mo.) Medical Society; fellow of the American College of Surgeons; a founder and at one time professor of abdominal surgery at the Kansas City College of Physicians and Surgeons; formerly professor of surgery at the Kansas City Post-Graduate Medical School and Hospital; health director of Kansas City, Mo., 1925-1926; a member of the staff of St. Luke's Hospital, of which he had been a founder, and of St. Joseph, St. Mary's and Kansas City General hospitals, where in 1916 he had been chief of staff; died June 10, aged 84, of myocarditis.

Alfred A. Kent Sr., Winter Park, Fla.; Jefferson Medical College of Philadelphia, 1885; formerly a practitioner in Lenoir, N. C.; member and past president of the Medical Society of the State of North Carolina; organizer and once president of the Caldwell County (N. C.) Medical Society; for many years a member of the North Carolina State Board of Medical Examiners and for two years president; served as a member of the North Carolina State Board of Health and the North Carolina state legislature; an organizer and former president of the Citizens Building and Loan Association and president of the First National Bank of Lenoir; died August 11, aged 85.

William H. German, Chicago; Michigan College of Medicine, Detroit, 1883; member of the Illinois State Medical Society and the American Association of Railway Surgeons; served as a major in the Illinois National Guard; formerly member of the Morgan Park elemeritary, high school and library boards; for twenty-two years secretary of the Calumet Park district; since 1902 local surgeon for the Chicago, Rock Island and Pacific Railroad; died in the Wesley Memorial Hospital July 31, aged 89, of chronic myocarditis, chronic nephritis and bilateral lobar pneumonia.

Smylie Scott Anderson, Hammond, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1906; served as health officer of Hammond; died June 25, aged 66.

Thomas Rufus Aycock ✠ Monroe, Ga.; University of Georgia Medical Department, Augusta, 1909; served as acting president and secretary of the Walton County Medical Society; on the staff of the Walton County Hospital, Walker Park; died in St. Joseph Infirmary, Atlanta, August 5, aged 62, of heart disease following an operation.

Charles Wesley Banks, East Orange, N. J.; Bellevue Hospital Medical College, New York, 1890; formerly city pathologist; served as chief of staff and chief surgeon of St. Mary's Hospital in Orange for many years; for many years in charge of the infirmary of the Thomas A. Edison, Inc., plant in West Orange; died July 21, aged 77, of carcinoma of the bladder.

John Banks, Hamilton, Ga.; Atlanta School of Medicine, 1911; died May 16, aged 65.

Blaine B. Barton, Markleysburg, Pa.; Maryland Medical College, Baltimore, 1905; member of the Medical Society of the State of Pennsylvania; died July 8, aged 64, of cerebral hemorrhage.

Burton Wayne Bivins, Wonewoc, Wis.; Chicago College of Medicine and Surgery, 1904; Spanish-American War Veteran; died in Chetek June 7, aged 68, of coronary thrombosis.

Stanislaus N. Borowiak, Buffalo; University of Buffalo School of Medicine, 1908; served as president of the board of education of Buffalo; secretary-treasurer of the Polish Medical Association, 1910-1914; in 1933 received the Polonia Restituta medal from the Polish government for aid in the restoration of Poland; died in the Millard Fillmore Hospital July 11, aged 61, of myocardial failure and coronary arteriosclerosis.

Oliver Preston Bourbon ✠ Los Angeles; Kansas City (Mo.) Hahnemann Medical College, 1908; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; formerly assistant professor of surgery (ophthalmology), College of Medical Evangelists; at one time lecturer on physiology at his alma mater; on the staffs of the Methodist Hospital and the California Hospital, where he died April 25, aged 80, of coronary thrombosis.

Christopher William Brown, Brooklyn; Long Island College Hospital, Brooklyn, 1903; member of the Medical Society of the State of New York; on the staff of the Bushwick Hospital for many years; during World War I served as a captain with the thirteenth Regiment Coast Artillery; died in the Long Island College Hospital July 7, aged 64, of carcinoma of the stomach with metastases to the spine.

Emerson Marrs Bushnell ✠ Black Lick, Pa.; University of Vermont College of Medicine, Burlington, 1903; president of the Indiana County Medical Society in 1936; school director and bank president; served on the staff of the Indiana Hospital, Indiana, Pa.; died April 21, aged 67, of coronary disease.

William Aaron Cashion, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; a captain in the medical corps of the U. S. Army during World War I; formerly associated with the U. S. Veterans Administration; died July 1, aged 53, of coronary occlusion due to cardiorenal vascular disease.

Charles Eli Caylor ✠ Bluffton, Ind.; Kentucky School of Medicine, Louisville, 1893; in 1895 president of the Wells County Medical Society; a charter member of the Bluffton Rotary Club; member of the Southern Medical Association; chief of staff of the Caylor-Nickel Clinic, which he founded, and of the Clinic Hospital, where he died July 5, aged 74, of a skull fracture and other injuries received in an automobile accident.

Emily Clark Charles, New York; New York Medical College and Hospital for Women, Homeopathic, New York, 1894; subsequently served at her alma mater as lecturer on diseases of children, assistant to the chair of diseases of children, secretary of the faculty, associate professor of diseases of children, professor of materia medica and dean; died in the Franklin County Hospital, Greenfield, Mass., July 9, aged 80, of a strangulated femoral hernia.

William Fladger Clark, Tampa, Fla.; Emory University School of Medicine, Atlanta, 1922; died in the Tampa Municipal Hospital July 11, aged 49, of bronchopneumonia and general septicemia.

Daniel Crosby ✠ Oakland, Calif.; Cooper Medical College, San Francisco, 1898; past president of the Alameda County Medical Association; fellow of the American College of Surgeons; health officer of Oakland, 1918-1920; past president of

the Insurance Association of Approved Hospitals; on the staffs of the Providence and Peralta hospitals, Oakland, and the Alameda Hospital, Alameda; died at his home in Piedmont July 15, aged 69, of coronary thrombosis.

Nelson Park Davis ✠ Pittsburgh; University of Pittsburgh School of Medicine, 1909; associate professor of surgery at his alma mater; fellow of the American College of Surgeons; on the staff of the Mercy Hospital; died July 7, aged 58, of cerebral hemorrhage.

Lester Cornelius Diddy, Paxton, Ill.; Chicago College of Medicine and Surgery, 1907; member of the Illinois State Medical Society; past president of the Ford County Medical Society; died July 11, aged 61, of coronary heart disease.

Hugh Victor Du Bois, Niota, Tenn.; Chattanooga (Tenn.) Medical College, 1904; died July 7, aged 64, of heart disease.

Harry Edward Dunlop ✠ Pelham, N. Y.; University of the City of New York Medical Department, New York, 1886; an Affiliate Fellow of the American Medical Association; died in the Gallagher Nursing Home, Mount Vernon, July 14, aged 80, of transverse myelitis and uremia.

Elihu Noble Elliott, Chicago; College of Physicians and Surgeons, Chicago, 1883; member of the Illinois State Medical Society; died June 29, aged 82, of carcinoma of the prostate with metastasis, pyelocystitis and cerebral arteriosclerosis.

Ralph Waldo Emerson, Owensville, Ind.; Eclectic Medical Institute, Cincinnati, 1898; died July 3, aged 74, of heart disease.

William Albert Fisher ✠ Chicago; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1885; at one time president and professor of ophthalmology at the Chicago Eye, Ear, Nose and Throat College; formerly professor of clinical ophthalmology at the University of Illinois College of Medicine; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; died July 31, aged 84.

Thomas Francis Foley, Buffalo; University of Buffalo School of Medicine, 1904; for many years staff physician in the child hygiene division of the city health department; a captain in the medical corps of the U. S. Army during World War I; medical examiner at the Attica State Prison; died July 11, aged 68, of pulmonary edema and dilatation of the heart.

Frederick Lewis Forker, Binghamton, N. Y.; University of the City of New York Medical Department, 1885; served as a member of the board of education; on the staffs of the Binghamton City and Our Lady of Lourdes Memorial hospitals; died July 11, aged 83, of arteriosclerosis.

William Hodskin Gale, St. Johns, Mich.; Jefferson Medical College of Philadelphia, 1901; formerly secretary and treasurer of the Clinton County Medical Society; served in the medical corps of the U. S. Army during World War I; in 1910 appointed to the U. S. Board of Pensions; for many years county health officer; on the staff of the Clinton Memorial Hospital; served as district surgeon for the Grand Trunk Railroad; died June 30, aged 74, of cardiorenal disease.

John Asa Gibbons, Mitchell, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1898; died in the Dunn Memorial Hospital, Bedford, July 6, aged 71, of carcinoma of the rectum.

John Louis Gilleland, Pullman, Wash.; American Medical College, St. Louis, 1903; member of the Washington State Medical Association; formerly on the staff of St. Ignatius Hospital, Colfax; died June 5, aged 69, of carcinoma of the prostate and Parkinson's disease.

Thomas Leverett Gingold, New Haven, Conn.; Columbia University College of Physicians and Surgeons, New York, 1919; formerly police surgeon and alderman; served on the staff of the Grace Hospital, where he died July 6, aged 49, of carcinoma of the pancreas.

Faustine Graves, Piney Flats, Tenn.; Tennessee Medical College, Knoxville, 1894; died July 13, aged 76, of myocardial failure and Parkinson's disease.

J. Edward Harmon, Pine Knot, Ky.; Hospital College of Medicine, Louisville, 1905; died in St. Anthony's Hospital, Louisville, June 29, aged 65, of hypertensive cardiovascular disease.

John Edward Harris, Winchester, Va.; Medical College of Virginia, Richmond, 1900; secretary-treasurer of the Medical Society of Northern Virginia and of the Winchester Memorial Hospital; died May 30, aged 69.

Atticus Greene Haygood ✠ Downey, Calif.; University of Nashville (Tenn.) Medical Department, 1891; Vanderbilt University School of Medicine, Nashville, 1891; a captain in the medical corps of the U. S. Army during World War I; examiner for the Selective Service Board; on the staff of the Methodist Hospital, Los Angeles; a charter member and past president of the Kiwanis Club; died in the Downey Community Hospital June 27, aged 73, of bronchopneumonia and acute gastroenteritis.

Edward Lathrop Hill Jr., Jacksonville, Ill.; St. Louis University School of Medicine, 1933; member of the Illinois State Medical Society; formerly an intern at St. Louis City Hospital and resident in neuropsychiatry at the City Sanitarium in St. Louis; first lieutenant in the medical reserve corps of the U. S. Army not on active duty; health officer in charge of the McDonough-Fulton bicounty health unit of the state health department with headquarters in Macomb; died in the Barnes Hospital, St. Louis, aged 37, of myelogenous leukemia.

Joseph Harrison Humphrey ✠ St. Louis; Washington University School of Medicine, St. Louis, 1901; served as director of hygiene for the board of education; died in the Evangelical Deaconess Home and Hospital June 23, aged 67, of cerebral embolism.

John Charles Kamp, Saugerties, N. Y.; University of Buffalo School of Medicine, 1895; member of the Medical Society of the State of New York; health officer since May 1924 with jurisdiction over the consolidated health district of Saugerties; served on the staff of the Kingston Hospital, Kingston; died June 18, aged 84, of arteriosclerosis.

Edwin Jerome Kauffman, Marion, S. D.; College of Physicians and Surgeons, School of Medicine of the University of Illinois, 1906; member of the South Dakota State Medical Association; formerly councilman; on the staffs of the Methodist State Hospital, Mitchell, and the Sioux Valley Hospital, Sioux Falls, where he died May 1, aged 60, of coronary thrombosis.

Theophilus Kubricht, Wallis, Texas; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; also a minister; died in a sanatorium in Houston May 28, aged 80.

Charles Labash, Passaic, N. J.; Chicago Medical School, 1926; member of the Medical Society of New Jersey; died in St. Mary's Hospital June 26, aged 61, of cirrhosis of the liver.

Virgil Alfred Lea, Gloster, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; died in the Marion Butler Memorial Hospital, Liberty, August 6, aged 63, of injuries received in an automobile accident.

Thomas B. W. Leland, San Francisco; University of California Medical Department, San Francisco, 1894; formerly county and city coroner; served as a lieutenant commander in the U. S. Navy during World War I; died June 28, aged 74.

Frederic Michael Lemen, Buffalo; University of Buffalo School of Medicine, 1905; member of the Medical Society of the State of New York; on the staff of the Millard Fillmore Hospital; died June 24, aged 64, of leukemia.

Patrick F. Martin, Emmitsburg, Md.; University of Maryland School of Medicine, Baltimore, 1900; member of the Medical and Chirurgical Faculty of Maryland; served as coroner in eastern and western health districts of Baltimore; for many years resident physician at the Mount St. Mary's College; died June 18, aged 67, of uremia.

Hubert Burns Marvin ✠ Binghamton, N. Y.; University of Buffalo School of Medicine, 1907; fellow of the American College of Physicians; examiner for draft board number 453; member of the examining board during World War I; on the staff of the Susquehanna Valley Home and the Binghamton City Hospital, where he died June 20, aged 64, of pneumonia.

Roy Cowles McDaniel ✠ Portland, Ore.; Medico-Chirurgical College of Philadelphia, 1905; fellow of the American College of Surgeons; served as secretary-treasurer of the Eastern Oregon District Medical Society; first vice president of the Oregon State Medical Society, 1909-1910; member of the staffs of St. Vincent's, Emanuel and Good Samaritan hospitals; died June 16, aged 62, of coronary occlusion.

Gertrude Minthorn, Newport, Ore.; State University of Iowa College of Medicine, Iowa City, 1910; formerly a medical missionary in India; died June 28, aged 62, of chronic endocarditis.

Edwin Pendleton Moon, Wetumpka, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1898; member of the Medical Association of the State of Alabama; served as state physician for prison number 1 and the tuberculosis hospital; died June 10, aged 67, of arteriosclerosis.

Nathan Vernon Noble, St. Mary's, Ohio; Starling-Ohio Medical College, Columbus, 1911; member of the Ohio State Medical Association; an officer in the medical corps of the U. S. Army during World War I; on the staffs of the Memorial and St. Rita's hospitals; died June 26, aged 55, of coronary thrombosis.

Carlton V. Norcross, Butte, Mont.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1887; died May 20, aged 80.

Clifford Seeley Page, Sisseton, S. D.; Yale University School of Medicine, New Haven, Conn., 1896; formerly coroner of Clark County, Neb., and camp surgeon for the Civilian Conservation Corps in New Ulm, Minn.; physician for the Indian agency; died in the Peabody Hospital, Webster, May 15, aged 68.

Howard Ashley Pardee, Upper Montclair, N. J.; University of the City of New York Medical Department, 1880; retired in 1934 as medical director of the United States Life Insurance Company, a position he held for many years; died July 23, aged 85, of acute congestive heart failure secondary to chronic myocarditis and arteriosclerosis.

Lester Claude Pepper ⊕ Sidney, Ohio; Starling Medical College, Columbus, 1898; formerly member of the legislative committee, past president, vice president, delegate and secretary of the Shelby County Medical Society; served as county coroner and as examining physician for the local Selective Service Board; died in the Wilson Memorial Hospital June 23, aged 68, of cerebral hemorrhage.

Carl Anton Platou, Valley City, N. D.; Maryland Medical College, Baltimore, 1912; member of the North Dakota State Medical Association; served during World War I; on the staff of the Mercy Hospital; died in Pompano, Fla., May 22, aged 56, of coronary occlusion.

Hyman Leon Ratnoff ⊕ New York; Cornell University Medical College, New York, 1906; on the staffs of the Beth-El and Kingston Avenue hospitals; died June 25, aged 62, of coronary thrombosis.

Volney E. H. Reed, Austin, Texas; Missouri Medical College, St. Louis, 1881; served as president of the bank in Holland for many years; formerly health officer of Milan County; died June 3, aged 84.

Clarence William Robertson ⊕ Jamestown, N. D.; Rush Medical College, Chicago, 1915; on the staffs of the Jamestown and Trinity hospitals; died May 22, aged 53, of coronary thrombosis.

Walter C. Robinson, Atlanta, Ga.; Southern Medical College, Atlanta, 1881; honorary member of the Medical Association of Georgia; died June 17, aged 88, of cerebral embolism.

CAPT. ELMER N. CARTER
M. C., A. U. S., 1911-1944

William Taylor Salmon, Duncan, Okla.; University of Tennessee Medical Department, Nashville, 1892; formerly associated with the Indian Service; died June 26, aged 75, of cranial hemorrhage and hypertension.

Charles Matthew Scott, Bluefield, W. Va.; University College of Medicine, Richmond, 1901; member of the West Virginia State Medical Association; fellow of the American College of Surgeons; past president of the county board of health; founder and head of St. Luke's Hospital; established the St. Luke's Nurses Training School; for eight years secretary of the state board of examiners for nurses; died in the University Hospitals, Iowa City, August 17, aged 65, of pneumonia following an operation.

John Sidney Sharp, Grenada, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1895; member of the Mississippi State Medical Association; for many years a member of the state board of health; member of the Grenada Clinic since its organization; on the staff of the Grenada General Hospital; chief surgeon in the area for the Illinois Central Railroad; died August 5, aged 72, of carcinoma of the prostate.

Isaac Judah Silverman ⊕ Washington, D. C.; University of Melbourne Faculty of Medicine, Australia, 1911; professor of clinical psychiatry at the Georgetown University School of Medicine; member of the American Psychiatric Association; fellow of the American College of Physicians; on the staff of the Gallinger Municipal Hospital; died August 6, aged 55, of acute myocardial infarction (posterior) and arteriosclerotic heart disease.

Rufus Southworth, Glendale, Ohio; Miami Medical College, Cincinnati, 1904; served as associate professor of therapeutics at the University of Cincinnati College of Medicine; served in the medical corps of the U. S. Army during World War I; formerly a medical missionary in China; made a memorable trip around the world in the schooner *Yankee*; formerly on the staff of the Cincinnati General Hospital; died in the Christ Hospital, Cincinnati, June 14, aged 65, of cerebral hemorrhage.

Vivienne Eu Gene McMains Spencer, Sterlington, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1930; served on the staff of St. Francis' Sanitarium, Monroe; died in El Paso, Texas, June 26, aged 39, of miliary tuberculosis.

Edward Charles Stoeltje, Rosebud, Texas; Louisville (Ky.) Medical College, 1897; member of the State Medical Association of Texas; killed in an automobile accident in Galveston June 20, aged 71.

Henry Marshall Swift ⊕ Cape Elizabeth, Maine; Harvard Medical School, Boston, 1900; assistant in neuropathology at Tufts College Medical School, Boston, 1907-1908; formerly professor of neurology at the Bowdoin Medical School, Portland; served during World War I; member of the American Psychiatric Association and the New England Society of Psychiatry; at one time on the staff of the Danvers Insane Hospital, Danvers, Mass.; past president of the Portland Medical Club; died August 18, aged 72.

Gaston E. Trosclair, Thibodaux, La.; University of the South Medical Department, Sewanee, Tenn., 1903; died in St. Joseph Hospital June 30, aged 67, of heart disease, nephritis and hypertrophic cirrhosis of the liver.

Thomas Freeman Turner ⊕ Macon, Mo.; Washington University School of Medicine, St. Louis, 1925; served an internship at St. Luke's Hospital, Kansas City; county physician; aged 42; drowned in Macon Lake June 28 when the motor boat in which he was riding capsized.

Elbert Lycurgus Watson ⊕ Newport, Ark.; Columbia University College of Physicians and Surgeons, New York, 1900; past president of the Arkansas State Board of Health; president of the Jackson County Medical Society; a captain in the medical corps of the U. S. Army during World War I; at one time mayor of Newport; served as county health officer; physician for the Missouri Pacific Railroad Company; died June 3, aged 68.

Myron La Verne White ⊕ Coffeyville, Kan.; Dunham Medical College, Chicago, 1901; served during World War I; died in the Mercy Hospital, Independence, June 4, aged 71, of cirrhosis of the liver and bronchopneumonia.

James Frederick Young, Danbury, Conn.; Columbia University College of Physicians and Surgeons, New York, 1913; served in the medical corps of the U. S. Army during World War I; died June 27, aged 55.

KILLED IN ACTION

Elmer Norval Carter, Huntington, W. Va.; Medical College of Virginia, Richmond, 1937; member of the West Virginia State Medical Association; served an internship at the Scott and White Hospital in Temple, Texas, a residency in psychiatry at the Spencer State Hospital, Spencer, and a residency in medicine at the Chesapeake and Ohio Hospital; commissioned a first lieutenant in the medical corps of the Army of the United States July 7, 1942 and began active duty on Aug. 10, 1942; in 1943 ordered to England, where he was assigned to hospital duty; promoted to captain; battalion surgeon in the Twenty-Ninth Division; killed in action in Normandy June 19, aged 32.

Bureau of Investigation

STIPULATIONS

Agreements Between Federal Trade Commission and Promoters of Various Products

Following are abstracts of stipulations in which promoters of "patent medicines," medical devices or cosmetics have agreed, following action by the Federal Trade Commission, to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products:

Amisogen.—In December 1943 J. P. Hoft, Berwyn, Ill., and the A. N. Baker Advertising Agency, Inc., Chicago, stipulated with the Federal Trade Commission that they would discontinue the following misrepresentations in the advertising of this product: That it will have any effect on asthma except to the extent that it may afford palliative relief from the paroxysms of this disease; that it will relieve hay fever or its symptoms, or that the product is free from opiates or narcotics. They further agreed not to disseminate any advertisement which fails to reveal that the product should not be used in excess of the dosage recommended, that frequent or continued use of it may be habit forming or cause nervousness, restlessness or sleeplessness and that the product should not be used by persons suffering from high blood pressure, heart disease, diabetes or thyroid trouble. It was provided, however, that such advertisements need only contain the statement, "Caution: Use Only as Directed" if the labeling directions contain a warning to the same effect.

Buxton's A Special Compound.—This is marketed by a Hope Buxton, trading as Buxton Medicine Company, Abbot Village, Maine. In November 1943 this person stipulated with the Federal Trade Commission to cease representing that the product has been approved by a federal agency, that it is a remedy or cure for sciatica, arthritis, neuritis, diseased liver, stomach or kidneys, that it eliminates uric acid from the system, overcomes acidity, strengthens the heart, normalizes the kidneys or bladder, purifies the blood or is a treatment for ingestion or stomach trouble.

Cramer Chemical Company's Preparations.—The concern in question, located at Gardner, Kan., stipulated with the Federal Trade Commission in December 1943 that it would discontinue the following misrepresentations: That "Nitrotan" is the best known or most universally used germicide in the United States, produces complete sterilization in 90 seconds, checks or stops bleeding other than capillary bleeding from superficial skin lesions, draws the torn, jagged edges of a wound together, stops sore throat, assists in the prevention of influenza, or may be relied on for quick and safe recovery from all skin conditions; that "Cramer's Athletic Stringent for Gargle" is effective in checking or preventing influenza, tonsillitis or like disorders; that "Cramer's Athletic Liniment" has special penetrating powers or reaches into muscular or other tissues to any significant degree; that "Cramer's Dextrose Tablets" will produce quick energy in the sense of capacity for more intense physical exertion, stimulate an athlete to greater performance, enable him to win more games, or afford immediate relief from hay fever or asthma; that "Cramer's Athletic Hair Oil" prevents "shower bath baldness" or any other kind of baldness; that "Iso-Pine" is a suitable preparation for sterilizing surgical instruments; that "Cramer's Athletic Effervescing Alkaline Powder" relieves acid condition of the system or has any significant effect on the acid-base balance of the body; that "Athletic Ointment" has any therapeutic effect on boils or performs any function in the healing process; that "Athletic Red Hot Ointment" relieves deep-seated pain or affords adequate relief from sprains; that "Athletic Analgesic Balm" relieves congestion; that "Athletic Foot Ointment" is an effective treatment for athlete's foot or ringworm except in mild cases; that "Athletic Inhalant" effectively relieves sinus trouble or forms a protective coating against bacteria; that "Cramer's Cold Tablets" have any appreciable effect in preventing common colds, or that "Cramer's Athletic Alkaline Powder" relieves nausea or stomach sickness, regardless of the nature or cause thereof. The respondent also agreed to cease using the word "Antiseptic" as part of the trade name or designation of "Cramer's Athletic Antiseptic Powder," or indicating in any way that the nostrum has antiseptic properties.

Dr. Gray's Foot Bath Powder.—In November 1943 S. W. Ward, trading as Ward & Sons, Chicago, entered into a stipulation with the Federal Trade Commission to discontinue the following misrepresentations in advertising the product: That it is used by physicians, hospitals or sanatoria; that it is a result of scientific research or a study of foot ailments; that statements in the advertising have been made by, or are quotations from, the literature of the United States Public Health Service, or that the latter or any other agency of the government has endorsed or recommended the use of this powder; that a package of it has a greater value than the price at which it is regularly sold; that its price is limited as to time, or that the powder draws poison from the feet, has curative or healing powers, or destroys germs. Ward further agreed to discontinue the representations that no other products are as effective as his powder is in the treatment of athlete's foot, itching, broken skin, open sores and blisters; that its use will prevent athlete's foot, or that the coloring of the skin caused by the powder destroys infection.

Elastic Rupture-Guard.—This is put out by a T. E. Brooks, trading as the Rupture-Guard Company, Marshall, Mich. In December 1943 Brooks and Ralph L. Wolfe & Associates, Inc., an advertising agency, stipulated with the Federal Trade Commission that they would discontinue representations that the device in question may be properly fitted to one's personal requirements when ordered through the mails; will hold the rupture securely or comfortably in any position of the body; will assist nature in strengthening the muscles or in closing the hernia opening, or that it is the only device of its kind; further, they would cease representing that the use of the device will eventually enable one to go without a truss or will correct or cure rupture; that it will stay in position under all conditions of use; that it is more natural or comfortable than other trusses, or that satisfaction in using it is guaranteed, unless the terms of the guaranty are disclosed.

Sar-Tol Cough Syrup, Cough Drops and Nose Drops.—On Dec. 8, 1943, the Federal Trade Commission reported that it had accepted a stipulation from O. B. Whitaker, trading as the O. B. Whitaker Manufacturing Company, Joplin, Mo. In this he agreed to cease representing that his preparations, whether used alone or in combination, prevent or cure colds, have any curative effect on the underlying factors which cause colds, or cure throat irritations, prevent fatigue, maintain health or aid in building body resistance. Further, he agreed to cease representing that Sar-Tol Cough Drops neutralize tobacco, onion or other odors. Also, Whitaker agreed to discontinue any advertisement which did not conspicuously warn that frequent or excessive use of the Nose Drops may cause injury to the lungs, nervousness, restlessness or sleeplessness; and should not, except on competent advice, be given to infants or young children, or be taken by persons suffering from high blood pressure, heart disease, diabetes or thyroid trouble. It was provided, however, that such advertisements need only contain the statement, "Caution: Use Only as Directed" if and when the directions in the labeling contain a warning to the same effect.

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the Federal Security Agency

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act, and in cases in which they refer to drugs and devices they are designated D.D.N.J. and foods, F.N.J. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the date of shipment; (4) the composition; (5) the type of nostrum; (6) the reason for the charge of misbranding, and (7) the date of issuance of the Notice of Judgment.]

Arabian Oil.—Standard Drug Company, Inc., Spartanburg, S. C. Shipped Feb. 28 and March 13, 1941. Composition: essentially a mixture of soap, ammonia, turpentine and water. Misbranded because the ammonia and turpentine present might be irritating to the skin, particularly if applied with rubbing, and also to eyes or mucous membranes, whereas label did not warn against this. Further misbranded because label falsely represented the product as a cure, treatment or preventive of pain incident to rheumatism, lame back, stiff joints, croup, swellings, wounds, and some other disorders.—[*D.D.N.J., F.D.C. 805; December 1943.*]

Climax C. & P. R.—Standard Drug Company, Inc., Spartanburg, S. C. Shipped Feb. 28 and March 13, 1941. Composition: essentially water, alcohol, chloroform and plant drugs, including capsicum. Misbranded because of false and misleading label representations for the product as a cure, treatment or preventive of pain in the bowels, cramp, colic and diarrhea.—[*D.D.N.J., F.D.C. 805; December 1943.*]

Gloria Tonic Tablets.—John A. Smith Company, Oconomowoc, Wis. Shipped Oct. 20, 1941. Composition: in each tablet 0.77 grain of iron, 3.64 grains of sodium salicylate, 0.003 grain of colchicin, and extract of cascara sagrada in an undeclared amount. Adulterated because strength differed from that which it was represented to possess, namely, in each tablet 1 grain of reduced iron, 5 grains of sodium salicylate and 1/250 grain of colchicin. Misbranded because directions on label did not provide for sufficient medication to constitute a treatment for gout; because, though a laxative, it failed to warn adequately that product should not be taken when symptoms of appendicitis were present, such as abdominal pain, nausea and vomiting, and that frequent or continued use might result in dependence on laxatives; also misbranded because statement "Tonic . . . An Allevial [sic] Treatment Useful in . . . Gout" was false and misleading, since the tablets, when used as directed, did not constitute a tonic or treatment for gout.—[*D.D.N.J., F.D.C. 762; September 1943.*]

Royale Agar and Oil with Phenolphthalein.—Vital Laboratories, Union City, N. J. Shipped Jan. 7 and March 21, 1942. Composition: an emulsion containing mineral oil and phenolphthalein. Misbranded in that it bore no labeling containing adequate directions for use, or the warning that it should not be taken when nausea, vomiting, abdominal pain or other symptoms of appendicitis are present, or the caution that frequent or continued use might result in dependence on laxatives. Further misbranded because name and place of business of manufacturer, packer or distributor were not given, or an accurate statement of the quantity of the contents or the common or usual name of each active ingredient.—[*D.D.N.J., F.D.C. 758; September 1943.*]

Correspondence

CANCER SAID TO BE CAUSED BY A SINGLE INJURY

To the Editor:—I am interested to note your editorial of August 12 on the matter of claims for disability said to have resulted from cancer caused by a single injury. In my opinion this editorial is timely but scarcely goes far enough. Traumatic cancer attracted my interest for a rather brief period following the death of the late Dr. James Ewing. Dr. Ewing had been interested in this matter for years and at his death a number of unfinished cases were turned over to me for completion.

In the course of hearings in these cases I acquired an exceedingly bad taste both for certain members of the legal profession and for members of the medical profession who seemed to me to be quite willing to testify to almost anything for a fee. I likewise learned to distrust the type of referee who is so afraid of possible injustice to a claimant that he tends to make awards in the face of incompetent evidence, and I believe he actually practices sociology rather than medicine. He rewards the "deserving" laborer at the expense of the insurance carrier and in so doing uses supposedly scientific medicine to further his notion of proper social behavior.

As for medical testimony, it appears to me that (1) such testimony can be purchased at a price or (2) those individuals who testify are hopelessly ignorant of the commonly known facts of cancer pathogenesis, which in turn is the result either of bad teaching in the cancer field or of dependence on casual statements heard in medical schools or encountered in textbooks on the subject. Lastly, it would oftentimes seem that the supposed expert doesn't take the trouble to reason at all. Let me illustrate: The same surgeon who will testify that mammary cancer has resulted from a single trauma will at the least provocation operate for a benign lesion of the breast and would never think of warning a patient that because of his operative trauma, which usually greatly exceeds the casual industrial trauma, she should give heed to the possibility that she will develop a cancer of the breast. The same surgeon who will do all sorts of orthopedic jobs involving chiseling into bone or insertion of such objects as ice tongs or pins or screws may testify that a blow which has left no real signs has caused an osteogenic sarcoma, although he never thinks his surgery will do so nor has he ever warned a patient with the severest form of bone trauma—a fracture—to be on the lookout for a possible sarcoma. A man testifies that a blow has caused a soft part sarcoma and yet that man and his colleagues throughout the world will do hundreds of thousands of appendectomies involving the cutting of abdominal wall musculature and observe no tumors. Another says that a malignant melanoma has followed a pin prick and yet no melanoma has ever followed the millions of venipunctures for complement fixation tests or intravenous medication. A third will say that testis cancer is the result of single trauma although the same tumor, histologically indistinguishable, appears in the ovary and no one assigns that to trauma. As far as I know I have never seen a cancer which I could logically and irrevocably assign to single trauma and, even more important than that, I do not know that any one has ever observed the development of a process which could be called "precancerous" after a trauma. The absurd efforts made in our compensation courts to emphasize the severity of traumas rests on the nonsensical point of view that there is some dividing line between the degree of trauma which will or will not cause cancer, under the popular supposition that the metabolic changes which make a cell a cancer cell require a few additional dynes for their complete florescence.

Some means should be found to exclude these figments of imagination from our compensation courts and place such claims in the hands of a truly expert commission—not composed of individuals who have nothing else to do or who have political friends either within medicine or without—and make the findings of this commission binding on the compensation referee, thus avoiding time wasted at hearings, questions and insults from cheap lawyers, and the mental anguish resulting from having to listen to the testimony of ignorant doctors, that in itself, judged by medicolegal standards, might be deemed a sufficient cause for development of a glioma in the expert. I tried this in a way. That is, I wrote a few letters to people who should have been interested and didn't get anywhere and am unable to wage a one man war on the racket. It will certainly be hard to break, for, under the law, compensation is profitable to claimant, physician and lawyer, and of course in the end the public foots the bill.

FRED W. STEWART, M.D., New York.
Acting Director, Memorial Hospital for the Treatment of Cancer and Allied Diseases.

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 8-12. Dr. W. L. Benedict, 102 Second Ave. S.W., Rochester, Minn., Secretary.

American Hospital Association, Cleveland, Oct. 2-6. Mr. George P. Bugbee, 18 East Division St., Chicago, Executive Secretary.

American Pediatric Society, Atlantic City, N. J., Sept. 25-27. Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis 8, Secretary.

American Public Health Association, New York, Oct. 3-5. Dr. Reginald M. Atwater, 1790 Broadway, New York 19, Executive Secretary.

American Roentgen Ray Society, Chicago, Sept. 24-29. Dr. H. Dabney Kerr, University Hospitals, Iowa City, Secretary.

Association of American Medical Colleges, Detroit, Oct. 23-25. Dr. Fred C. Zapffe, 5 S. Wabash Ave., Chicago, Secretary.

Association of Military Surgeons of the United States, New York, Nov. 2-4, Col. James M. Phalen, Army Medical Museum, Washington 25, D. C., Secretary.

Colorado State Medical Society, Denver, Sept. 27-29. Dr. John S. Bouslog, 537 Republic Bldg., Denver 2, Secretary.

Delaware, Medical Society of, Lewes, Sept. 11-12. Dr. W. O. La Motte, 601 Delaware Avenue, Wilmington, Secretary.

District of Columbia, Medical Society of the, Washington, Oct. 5-7. Mr. Theodore Wiprud, 1718 M St. N.W., Washington, Secretary.

Indiana State Medical Association, Indianapolis, Oct. 3-5. Mr. T. A. Hendricks, 23 East Ohio St., Indianapolis 4, Executive Secretary.

Inter-State Postgraduate Medical Association of North America, Chicago, Oct. 17-20. Dr. Arthur G. Sullivan, 16 N. Carroll St., Madison, Wis., Managing Director.

International College of Surgeons, U. S. Chapter, Philadelphia, Oct. 3-5. Dr. Desiderio Roman, 250 South 17th St., Philadelphia, Secretary.

Kentucky State Medical Association, Lexington, September 18-20. Dr. P. E. Blackerby, 620 S. Third St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 27-29. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.

Mississippi Valley Medical Society, Peoria, Ill., Sept. 27-28. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

Omaha Mid-West Clinical Society, Omaha, Nebraska, Oct. 23-27. Dr. J. D. McCarthy, 1036 Medical Arts Bldg., Omaha 2, Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Sept. 19-21. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh 22, Secretary.

Radiological Society of North America, Chicago, Sept. 24-29. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.

Virginia, Medical Society of, Richmond, Oct. 23-25. Miss Agnes V. Edwards, 1200 E. Clay St., Richmond 19, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 18-20. Mr. Charles H. Crownhart, 110 E. Main St., Madison 3, Secretary.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Cerebral Hemorrhage Following Exertion in Hot Weather by Syphilitic Workman.—The workman, a Negro about 40 years of age, had syphilis in the tertiary state. The court nevertheless states that he enjoyed good health prior to the date of the industrial accident here discussed. On May 1, 1942, a "very warm" day, he had been unloading lumber from boxcars. About 7 p. m. he became overheated and had a dizzy feeling but continued to work another hour until his work day was finished. He was sick at home all night but returned to work next morning, when he became unconscious and was unable to begin work. Subsequently he suffered a cerebral hemorrhage which resulted in paralysis of his left side. He was denied compensation under the Flordia workmen's compensation act and appealed to the circuit court, Leon County, which affirmed the denial of compensation. He then appealed to the Supreme Court of Florida.

The Florida workmen's compensation act, said the Supreme Court, so far as here pertinent, provides as follows:

> "Accident" shall mean only an unexpected or unusual event, happening suddenly. . . . Where a preexisting disease is accelerated or aggravated by an accident arising out of and in the course of the employment, only acceleration of death or the acceleration or aggravation of disability reasonably attributable to the accident shall be compensable.

On just what precise reason the trial court denied compensation is not clear. Presumably the employer and his insurance carrier must have argued that Davis's disability was due solely to the syphilitic condition and that there was no causal connection between the exertion of employment and the disability. The Supreme Court concluded that Davis was entitled to compensation on the theory that the exertion of his employment had accelerated or aggravated his syphilitic condition. The court relied, among other cases, on *Crowley's Case*, 223 Mass. 288, 111 N. E. 786. The Massachusetts statute, said the Supreme Court, was similar to the Florida statute to be construed. In that case also the employee had syphilis but, being dormant, it left his ability unimpaired to carry on his work. Exertion of employment, apparently, was followed by paralysis or insanity and total disability. The employer and his insurance carrier contended that the workman could not recover under the Massachusetts workmen's compensation act because of the preexisting syphilitic condition. The court there said:

> The statute prescribes no standard of fitness to which the employee must conform, and compensation is not based on any implied warranty of perfect health, or of immunity from latent and unknown tendencies to disease, which may develop into positive ailments, if incited to activity through any cause originating in the performance of the work for which he is hired. What the legislature might have said is one thing, what it has said is quite another thing, and in the application of the statute the cause of partial or total incapacity may spring from and be attributable to the injury just as much where undeveloped and dangerous physical conditions are set in motion producing such result as where it follows directly from dislocations; or dismemberments; or from internal organic changes capable of being exactly located. *Madden's Case*, 222 Mass. 487, 111 N. E. 379.

Recovery of compensation by a claimant, continued the Florida court, is not conditioned on good or perfect health. The statute here considered does not require a health certificate or require the workman to be free from disease at the time he was employed or injured. It is reasonable to assume that a workman has physical infirmities and takes them, if any, with him to his employment. The employer accepts the workman in such physical condition as he finds him and assumes the risk of a disease condition aggravated by injury. Compensation is not made to depend on the condition of health of the workman but on an injury which is a hazard of employment. The controlling principle of law is succinctly expressed by Schneider on Workmen's Compensation Law, ed. 2, vol. 1, p. 517, par. 138, viz:

> Aggravation of Preexisting Condition.—"Likewise the courts, consistent with the theory of workmen's compensation acts, hold with practical uniformity that, where an employee afflicted with disease receives a personal injury under such circumstances as that he might have appealed to the act for relief on account of the injury had there been no disease involved, but the disease as it in fact exists is by the injury materially aggravated or accelerated, resulting in disability or death earlier than would have otherwise occurred and the disability or death does not result from the disease alone progressing naturally, as it would have done under ordinary conditions, but the injury aggravating and accelerating its progress, materially contributes to hasten its culmination in disability or death, there may be an award under the compensation acts."

The Supreme Court accordingly, in effect, ordered an award of compensation in favor of the workman.—*Davis v. Artley Const. Co., 18 So. (2d) 255 (Fla., 1944).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the Examining Boards in Specialties were published in THE JOURNAL, Sept. 2, page 49.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, Oct. 24-26. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.
ARIZONA: * Phoenix, Oct. 3-4. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.
ARKANSAS: * Little Rock, Nov. 9-10. Sec., Dr. D. L. Owens, Harrison.
DELAWARE: Dover, Oct. 10-12. Sec., Medical Council of Delaware, Dr. J. S. McDaniel, 229 S. State St., Dover.
DISTRICT OF COLUMBIA: * Washington, November. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.
IDAHO: Boise, Jan. 8-11. Dir., Bureau of Occupational Licenses, Mrs. Lela D. Painter, 355 State Capitol Bldg., Boise.
ILLINOIS: Chicago, Oct. 10-12. Supt. of Registration, Department of Registration and Education, Mr. Philip Harman, Springfield.
INDIANA: Indianapolis, Jan. 3-5. Exec. Sec., Board of Medical Registration and Examination, Miss Ruth V. Kirk, 301 State House, Indianapolis 4.
IOWA: * Iowa City, Sept. 25-27. Dir. Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.
KANSAS: Nov. 2-3 Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.
KENTUCKY: Louisville, Sept. 11-13. Sec., State Board of Health, Dr. Philip E. Blackerby, 620 S. Third St., Louisville.
MARYLAND: *Homeopathic.* Baltimore, Dec. 1-3. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.
MICHIGAN: * Detroit, Sept. 25-27. Sec., Board of Registration in Medicine, Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.
MISSISSIPPI: Jackson, Oct. 16-17. Asst. Sec., Dr. R. N. Whitfield, Jackson.
MISSOURI: St. Louis, Sept. 18-20. Sec., State Board of Health, Dr. James Stewart, State Capitol Bldg., Jefferson City.
MONTANA: Helena, Oct. 2-4. Sec., Dr. O. G. Klein, First Nat'l. Bank Bldg., Helena.
NEBRASKA: * Omaha, Sept. 26-28. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.
NEW HAMPSHIRE: Concord, Sept. 14-15. Sec., Board of Registration in Medicine, Dr. D. G. Smith, 77 Main St., Nashua.
NEW MEXICO: * Santa Fe, Oct. 9-10. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.
NORTH CAROLINA: Raleigh, Sept. 11-12. Sec., Dr. W. D. James, Hamlet.
NORTH DAKOTA: Grand Forks, Jan. 2-5. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.
OHIO: *Examination.* Columbus, Sept. 26-29. *Endorsement.* Columbus, Oct. 3. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.
OKLAHOMA: * Oklahoma City, Sept. 16. Sec., Dr. J. D. Osborn, Jr., Frederick.
SOUTH CAROLINA: Charleston, Sept. 11-13. Sec., Dr. N. B. Heyward, 1329 Blandena St., Columbia.
SOUTH DAKOTA: * Pierre, Jan. 16-17. Sec., Medical Licensure, State Board of Health, Dr. G. Cottam, Pierre.
TENNESSEE: * Memphis and Nashville, Sept. 20-22. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis 3.
TEXAS: Dallas, Nov. 15-17 and Dec. 19-21. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas 2.
UTAH: Salt Lake City, Sept. 13-15. Asst. Dir., Department of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.
VERMONT: Burlington, Sept. 12-14. Sec., Dr. F. J. Lawliss, Richford.
VIRGINIA: Richmond, Sept. 19-22. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.
WEST VIRGINIA: Charleston, Oct. 2-4. Commissioner, Public Health Council, Dr. John E. Offner, State Capitol, Charleston 5.
WISCONSIN: * *Endorsement.* Milwaukee, Sept. 18-19. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: New Haven, Oct. 14. Address: State Board of Healing Arts, 250 Church Street, New Haven 10.
DISTRICT OF COLUMBIA: Washington, Oct. 23-24. Sec., Commission on Licensure, Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.
FLORIDA: Gainesville, Nov. 4. Final date for filing application is Oct. 20. Sec., Dr. J. F. Conn, John B. Stetson University, DeLand.
IOWA: Des Moines, Oct. 10. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.
MICHIGAN: Ann Arbor and Detroit, Oct. 13-14. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.
NEBRASKA: Omaha, Oct. 3-4. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.
NEW MEXICO: Santa Fe, Feb. 12. Sec., Miss Marion M. Rhea, State Capitol, Santa Fe.
OREGON: Portland, Nov. 4. Sec., Mr. C. D. Byrne, University of Oregon, Eugene.
TENNESSEE: Memphis and Nashville, Sept. 25-26. Sec., Dr. O. W. Hyman, 874 University Ave., Memphis.
WISCONSIN: Madison, Sept. 23. Sec., Prof. R. N. Bauer, 152 W. Wisconsin Ave., Milwaukee 3.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1934 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Archives of Dermatology and Syphilology, Chicago

49:389-478 (June) 1944

Keratosis Blennorrhagica Without Gonorrhea (Reiter's Disease?). W. F. Lever and G. M. Crawford.—p. 389.
Chromoblastomycosis: Report of Case from Continental United States and Discussion of Classification of Causative Fungus. C. H. Binford, G. Hess and C. W. Emmons.—p. 398.
*Intensive Ambulatory Therapy of Syphilis: Thirty Day Mapharsen Technic. S. Goldblatt.—p. 403.
Ulcerative Diphtheria of Skin: Sporadic and Epidemic Types Observed in Haifa, Palestine. S. Gill.—p. 408.
*Hereditary Ectodermal Dysplasia: Report of Case, with Experimental Study. Z. Felsher.—p. 410.
Localized Myxedema in Association with Hyperthyroidism. J. C. Amersbach and B. Kanee.—p. 415.
Fixed Erythema Due to Sulfanilamide with Gradually Lessening Sensitivity. A. Dostrovski and F. Sagher.—p. 418.
Coal Tar in Dermatologic Preparations. J. G. Downing, L. M. Ohmart and G. Di Cicco.—p. 421.
Bullous Lichen Sclerosus et Atrophicus: Its Relation to Bullous Scleroderma. C. R. Anderson.—p. 423.
Cutaneous Absorption: II. Value of Petrolatum, Anhydrous Wool Fat and Other Bases in Percutaneous Absorption of Topically Applied Cottonseed Allergen. A. Walzer and S. S. Sack.—p. 427.
*Contact Dermatitis from Cold Permanent Waving. J. B. Howell.—p. 432.
Cutaneous Leishmaniasis (Oriental Sore): I. Time Required for Development of Immunity After Vaccination. D. A. Berberian.—p. 433.

Thirty Day Mapharsen Technic in Syphilis.—Goldblatt gave 60 mg. of mapharsen intravenously dissolved in 5 cc. of sterile distilled water for thirty successive days. A total of 1,800 mg. of mapharsen was thus administered without adjuvant therapy. An unselected group of 107 patients with syphilis of all types was treated by this intensive consecutive thirty day mapharsen method. The serologic reactions, which were positive in 81 per cent of the total group before treatment, showed a decided and continuing reduction in titer. On termination of the treatment positive serologic reactions were noted in 55 per cent, two months later in 35 per cent. Follow-up investigations from three to six months after the treatment indicated that the reactions of 20 per cent remained positive. No significant changes were observed in the formed or chemical constituents of the blood. Electrocardiographic examination revealed no deleterious effect on cardiac function, either immediately or remotely. Roentgenographic examination of the cardiovascular system indicated no progressive or toxic sequelae. Retreatment was carried out for the 3 patients with serologic relapse. Two with severe meningovascular involvement were subjected to fifteen attacks of induced fever concurrent with the hyperintensive therapy without untoward reaction. It was found possible to administer sulfonamide compounds for the treatment of intercurrent disease without interrupting the intensive mapharsen therapy. Complete healing of all the lesions of infectious syphilis required an average of ten days. A gain in weight and increased appetite and feeling of well-being were noted in the large majority of patients. No mucocutaneous relapse or neurorecurrence developed. This therapy appears to be nontoxic. Hospitalization is not required; the treatment is inexpensive and does not disrupt the economic life of the patient.

Hereditary Ectodermal Dysplasia.—Felsher shows that the inheritance of hereditary ectodermal dysplasia is not as clearcut as was believed. The history of his patient with this disorder revealed sex linked inheritance in the family tree, with male patients and female conductors. Eccrine glands were practically absent on the face and abdomen. Their number on the extremities was decreased to 5 to 7 per cent of the normal number. Apocrine sweat glands were abundant in the axillas, on the upper part of the chest and on the perimamillary areas. The patient's insensible perspiration, at rest in a room temperature of 73 F., was normal. Atropine sulfate in a dose of 0.5 mg. subcutaneously did not change it. The intradermal injection of a 1:100 solution of acetylcholine bromide produced only a few isolated spots of sweating on the patient's forearm, as contrasted with the decided response of a normal control subject. In the heat chamber the body temperature of the patient rose rapidly whereas the body temperature of normal persons did not change under similar conditions. The term "hypohidrotic" is suggested as being more accurate than "anhidrotic" for the described type of ectodermal dysplasia. The absence of eccrine glands is not necessarily complete in spite of hyperthermia at high external temperatures.

Contact Dermatitis from Cold Permanent Waving.—Howell reports that a woman experienced burning and stinging sensations over the sides of her neck, face and ears the afternoon after she had received her first cold permanent wave. The next morning she noted redness of the areas. When she was in the office the following day a mild dermatitis venenata type of eruption, consisting of slight swelling, diffuse redness, pruritus and in some areas fine vesiculation, was noted. The dermatitis reached its maximum extent within seventy-two hours and subsided by the end of the sixth day. Patch tests on 3 normal controls with 1 per cent concentrations of the shampoo, the preliminary lotion, the waving compound, the neutralizing solution and mixtures of these chemicals failed to evoke any reactions. Contact tests were then applied to the forearm of the patient one month after the dermatitis of her face, neck and ears had healed. On two different occasions a positive reaction followed within twenty-four hours the application of the preliminary lotion. No reactions were observed following contact tests with the waving compound, the neutralizing liquid or the shampoo. This case is an example of an eczematous contact dermatitis following within twenty-four hours a "cold permanent wave." Unquestionably this patient was already sensitive to some ingredient in the preliminary lotion, since patch tests elicited positive reactions on two different occasions. Sensitization due to previous contacts with the allergen present in the preliminary solution or a closely related chemical took place without the patient's knowledge. Reexposure to this substance when she received a cold permanent wave precipitated the allergic response.

Archives of Otolaryngology, Chicago

39:465-572 (June) 1944

Four Decades of Nasal Allergy. L. Richards.—p. 465.
Sarcoid of Nose. R. Fletcher.—p. 470.
*p*H of Nasal Secretions in Situ in Atrophic Rhinitis: Its Implications. N. D. Fabricant.—p. 474.
Reconstruction of Deformed Nasal Septum: Critical Evaluation of Orthodox Submucous Resection from an Anatomophysiologic Standpoint. M. S. Ersner.—p. 476.
Osteomyelitis of Frontal Bone. L. A. Brown.—p. 485.
Recent Progress in Management of Acute Suppuration of Middle Ear. J. R. Lindsay.—p. 492.
Head Noises in Normal and in Disordered Ears: Significance, Measurement, Differentiation and Treatment. E. P. Fowler.—p. 498.
Atmospheric Pressures in Nasal Fossa, Maxillary Sinus and Trachea. E. Simon.—p. 504.
Physiology of Nose from Standpoint of Plastic Surgeon. A. W. Proetz.—p. 514.
Role of Plastic Surgery in Field of Otolaryngology. S. Fomon.—p. 518.
Report of Isograft Transplants in Identical Twins. A. Schattner.—p. 521.
*Injection of Tympanum for Chronic Conductive Deafness and Associated Tinnitus Aurium: Preliminary Report on Use of Ethylmorphine Hydrochloride. B. C. Trowbridge.—p. 523.
Perforation of Tuberculous Lymph Nodes into Trachea and Bronchi. O. Auerbach.—p. 527.
Adenoma of Ceruminous Glands. H. J. Adler and I. Sommer.—p. 533.
Use of Solution of Posterior Pituitary of Twice U. S. P. Concentration for Hemorrhage Following Tonsillectomy or Adenoidectomy. J. W. McLaurin.—p. 536.
Contributions to Plastic Surgery During 1943. L. A. Peer.—p. 537.

Injection of Tympanum for Chronic Conductive Deafness and Tinnitus Aurium.—According to Trowbridge, injection of the tympanum as a method of treatment in deafness was first suggested and used by Gray in 1934 at the Middlesex Hospital in London. Gray advocated this therapy for otosclerosis and employed thyroxin as the medium of injection.

Results with thyroxin therapy have not been altogether encouraging. Trowbridge sought an agent which would incite a sterile inflammation with subsequent absorption of the scar tissue, cicatricial bands and adhesions that interfere with the normal functioning of the conductive mechanism. The therapeutic value of ethylmorphine hydrochloride in removing pupillary exudates and in absorbing interstitial corneal deposits has long been known. It acts as a vasodilator and lymphagogue, stimulating the vascular and lymphatic circulation of the eye and producing dilatation of these vessels. The drug produces analgesia, which counteracts the discomfort of the injection and of the subsequent inflammation. Improvement in hearing occurred in 18 of 22 patients selected for this type of therapy. In 4 patients no improvement was obtained. Lessening of the tinnitus occurred in 6 and loss of tinnitus in 3 of 9 patients with associated tinnitus aurium. All of the patients were ambulatory and continued their usual daily routines without interference from the injections. Secondary reactions were negligible. Only transient vertigo occurred in several cases, disappearing within fifteen minutes after the injection. The improvement in hearing was demonstrated by audiometric studies as well as by the testimony of the patients themselves.

Connecticut State Medical Journal, Hartford

8:343-406 (June) 1944

Medical Practice and Hospital Service. A. M. Schwitalla.—p. 348.
Carcinoma of Lip at New Haven Hospital, 1921 to 1940, Inclusive. E. A. Lawrence and A. W. Oughterson.—p. 353.
Some Fallacies and Deficiences in Problem of Heart Disease. W. J. Bruckner.—p. 357.
Purposes of Woman's Auxiliary. Mrs. E. J. Carey.—p. 360.

8:407-482 (July) 1944

Comment on Experimental Gastric Cancer. G. M. Smith.—p. 409.
Treatment of Thoracic Trauma. G. E. Lindskog.—p. 414.
Bacillary Dysentery. K. M. Wheeler.—p. 419.
Osteomyelitis of Skull. B. S. Brody.—p. 421.
How Hospitals Are Attempting to Meet Increasing Demands for Hospital Service. O. H. Bartine.—p. 423.
Report on Progress and Activities of the Society. J. R. Miller. —p. 426.

Hawaii Medical Journal, Honolulu

3:159-198 (March-April) 1944

Anesthesia in Small Hospital: Review of Methods Used for Period of One Year. M. A. Brennecke.—p. 159.
Primary Carcinoma of Liver with Hemorrhage: Report of Case. C. T. Young.—p. 161.
Rupture of Uterus Following Previous Cesarean Section: Review and Report of 2 Cases. C. F. Chang and W. K. Chang.—p. 164.

Iowa State Medical Society Journal, Des Moines

34:225-268 (June) 1944

Head Injuries. A. Ver Brugghen.—p. 225.
Continuous Caudal Anesthesia. D. Wall.—p. 236.
Mental Hygiene Program for Iowa. M. Heiman.—p. 238.
Clinical Diagnosis of Pernicious Anemia. F. P. McNamara.—p. 242.

34:269-340 (July) 1944

Postwar Industrial Medical Program. C. D. Selby.—p. 269.
Military Management of Allergic Diseases. S. W. French and L. J. Halpin.—p. 272.
Hard of Hearing and Hearing Aids. C. C. Walker.—p. 274.
Mixed Tumor of Parotid Gland. A. B. Nesler.—p. 276.

Journal of Experimental Medicine, New York

79:559-680 (June) 1944

Experimental Epidemiology of Tuberculosis: Prevention of Natural Air Borne Contagion of Tuberculosis in Rabbits by Ultraviolet Irradiation. M. B. Lurie, with collaboration of Helen Tomlinson and S. Abramson.—p. 559.
Recoverability of Virus from Papillomas Produced Therewith in Domestic Rabbits. W. F. Friedewald and J. G. Kidd.—p. 591.
Amino Acid Mixtures Effective Parenterally for Long Continued Plasma Protein Production: Casein Digests Compared. S. C. Madden, R. R. Woods, F. W. Shull and G. H. Whipple.—p. 607.
Methionine Protects Against Mapharsen Liver Injury in Protein Depleted Dogs. J. P. B. Goodell, P. C. Hanson and W. B. Hawkins. —p. 625.
Qualitative Differences in Antigenic Composition of Influenza A Virus Strains. W. F. Friedewald.—p. 633.
Studies on Etiology of Primary Atypical Pneumonia: Filtrable Agent Transmissible to Cotton Rats, Hamsters and Chick Embryos. M. D. Eaton, G. Meiklejohn and W. van Herick.—p. 649.

Journal of National Malaria Society, Tallahassee, Fla.

3:79-154 (June) 1944

*Malaria Mortality and Morbidity in United States for Year 1942. E. C. Faust.—p. 79.
Recent Research in Prophylaxis and Treatment of Malaria: Report for 1942-1943. H. C. Clark.—p. 85.
Recent Research in Avian and Simian Malaria. R. I. Hewitt.—p. 95.
Malaria Prevention Activities of State Boards of Health, 1943. F. J. Underwood.—p. 111.
Introduction of Tropical Diseases Other Than Malaria Into United States After the War. W. A. Sawyer.—p. 115.
Spleen Measurement in Malaria. L. W. Hackett.—p. 121.
Notes on Construction and Use of Stable Traps for Mosquito Studies. M. Bates.—p. 135.

Malaria Mortality and Morbidity in 1942.—Malaria mortality data by states and counties for the United States in 1942 show a continued improvement over previous years. Only eight states had a rate of 1.0 or more per hundred thousand and only four counties had a rate of 25.0 or more. The malaria morbidity data, as reported by bureaus of vital statistics of the several states, continue to be unreliable when tested against the expected ratios of deaths to cases. In mildly endemic territory, such as the malarious areas of the United States have become, it is estimated that there were between 236,000 and 590,000 cases in 1942 as compared with 278,000 to 695,000 in 1941.

Journal of Nervous and Mental Disease, New York

99:889-1012 (June) 1944

Prevention of Subconvulsive Reactions in Convulsive Therapy for Psychoses. Esther S. Ziskind and E. Ziskind.—p. 889.
Cholinergic Sensitivity. R. Altschul.—p. 895.
Myotonic Dystrophy. B. B. Mongillo and M. Serog.—p. 906.
"Shock" Therapies. G. H. Alexander.—p. 922.
Suggestions for New Therapy in Dementia Precox. E. Lowenstein. —p. 925.
Diethylstilbestrol in Management of Psychopathological States in Males. R. M. Foote.—p. 928.
Growth Concept of Nervous Integration: IV. On Etiology and Treatment of Renal Hypertension. D. E. Schneider.—p. 936.
Homosexuality, Transvestism and Psychosis. S. Liebman.—p. 945.
The "Placing-Into-Mouth" and Coprophagic Habits. S. Arieti.—p. 959.

Journal of Neurosurgery, Springfield, Ill.

1:163-226 (May) 1944

Neurosurgical Head Rest for Use in Army and Navy Hospitals. W. M. Craig.—p. 163.
Traumatic Pneumocephalus with Spontaneous Ventriculogram: Report of Case. A. Kaplan.—p. 166.
*Studies on Fibrin Foam as Hemostatic Agent in Neurosurgery, with Special Reference to Its Comparison with Muscle. F. D. Ingraham, O. T. Bailey and F. E. Nulsen.—p. 171.
Experimental Traumatic Cerebral Cysts in Rabbit. M. A. Falconer and Dórothy S. Russell.—p. 182.
Mechanics of Trauma, with Special Reference to Herniation of Cerebral Tissue. A. H. S. Holbourn.—p. 190.
Intracranial Dural Cyst, with Report of Case. W. Haymaker and M. E. Foster Jr.—p. 211.
*Sutureless Reunion of Severed Nerves with Elastic Cuffs of Tantalum. P. Weiss.—p. 219.

Fibrin Foam as Hemostatic Agent in Neurosurgery.—Ingraham and his associates show that in the course of fractionation of human blood plasma large quantities of human fibrinogen and thrombin become available. Bering has prepared from these materials a substance designated "fibrin foam." The product is composed of a porous mass of fibrillar fibrin with macroscopic air spaces. When the foam is moistened, fluid rapidly enters the air spaces. It then becomes rubbery and shrinks to a certain extent. If the moistening agent is a solution of human thrombin, the foam becomes an effective hemostatic agent. While the fibrin foam and thrombin may be used in many forms of surgery, the authors' experiences are limited to neurosurgery. In this field it has proved the most satisfactory hemostatic agent available. For use in the operating room two bottles are provided. One contains sterile fibrin foam and the other thrombin in the dry state. Thrombin is dissolved in 30 cc. of sterile isotonic solution of sodium chloride. Pieces of the fibrin foam are then placed in the thrombin solution, after which the material is ready for use. For application to bleeding surfaces a piece of appropriate size is cut and held firmly against the tissue. This is usually best accomplished by covering it with a cotton pattie and applying suction for a moment. When the pattie is removed, the fibrin foam remains adherent to the tissue surface. The authors found that fibrin foam with

thrombin promptly controls bleeding from oozing surfaces, from large veins and from the dural sinuses. Muscle as a hemostatic agent is less adaptable than fibrin foam and causes considerably more tissue reaction. Fibrin foam has several advantages over soluble cellulose, though the tissue reaction to the two substances is similar. Fibrin foam has been applied at more than one operation in 34 cases without change in tissue response or other damage. The usefulness of fibrin foam is enhanced by the fact that it may be molded to the contour of the bleeding surface before or after application, that it retains that contour after pressure is released and that it adheres quickly and permanently to the bleeding surface.

Sutureless Reunion of Nerves with Elastic Cuffs of Tantalum.—Weiss describes a method by which tantalum foil can be fashioned into resilient self-sealing tubes, which may be used as cuffs for the sutureless linking of severed nerve stumps in the manner previously described for arterial sleeves. Preliminary observations on monkey and cat nerves joined by this method have demonstrated that excellent reunion between the stumps with the properties required for optimal nerve regeneration may be achieved if the sleeves have been suitably shaped and properly handled.

Journal of Thoracic Surgery, St. Louis

13:169-270 (June) 1944

Dermoid Cysts and Teratomas of Mediastinum: Review. N. L. Rusby. —p. 169.
Closed Intrapleural Pneumolysis. J. Goorwitch.—p. 223.
Surgical Management of Residual Tuberculous Cavities Following Primary Thoracoplasty. A. R. Judd.—p. 249.
Pneumolysis Sponge Carrier and Dissector. J. S. Conant.—p. 267.

Journal of Urology, Baltimore

51:447-562 (May) 1944

Bilateral Nephrolithiasis in Horseshoe Kidney. F. Farman.—p. 447.
Duplication of Kidney and Ureter: Statistical Study of 230 New Cases. E. F. Nation.—p. 456.
Congenital Renal Hypoplasia Associated with Hypertension: Report of 2 Cases. D. R. Higbee.—p. 466.
Case of Polycystic Kidney Disease with Unusual Features. R. Schwartz. —p. 476.
Two Stage Nephrectomy. G. V. Caughlan and T. D. Boler.—p. 481.
Renal Surgery as Cause of Renal Ischemia. W. G. Hayward.—p. 486.
Giant Hydronephrosis Following Generalized Trauma. M. Meltzer. —p. 491.
*Carcinoma of Bladder: An Improved Technic for Cystoscopic Implantation of Radium Element. T. D. Moore.—p. 496.
Rhabdomyosarcoma of Urinary Bladder: Clinicopathologic Case Report, with Review of Literature, Including Tabulation of Rhabdomyosarcoma of Prostate. E. N. Khoury and F. D. Speer.—p. 505.
Extramural Rhabdomyosarcoma of Neck of Urinary Bladder. E. F. Hirsch and G. W. Gasser.—p. 517.
Interstitial Cystitis: Treatment with Silver Nitrate. T. L. Pool and H. F. Rives.—p. 520.
My Personal Opinions of Interstitial Cystitis (Hunner's Ulcer). T. L. Howard.—p. 526.
Sympathetic Innervation of Detrusor Muscle. A. Kuntz and G. Saccomanno.—p. 535.
Primary Fibrosarcoma of Penis: Review of Literature and Report of Case. C. A. Wattenberg.—p. 543.
Hemangioma of Testis. A. H. Kleiman.—p. 548.
Torsion of Spermatic Cord. E. E. Ewert and H. A. Hoffman.—p. 551.

Cystoscopic Implantation of Radium Element in Carcinoma of Bladder.—Moore states that cases suitable for closed methods of treatment, with or without the use of radium, must be selected with care. They comprise chiefly tumors of a low degree of malignancy, and occasionally small or early tumors of grades 3 and 4. In a series of 96 cases of carcinoma of the bladder, 16 were inoperable and treatment was refused in 10. Of the 70 patients who underwent treatment, 36 were treated by closed methods and 34 were subjected to open operation. If cystoscopic implantation of radium is contemplated, the tumor should be in a location favorable for a good view and for attack through a direct cystoscope, which would include tumors involving the trigone, lateral bases, posterior wall and the posterior half of the lateral walls. If the growth is in the vesical dome, the anterior wall or anterior half of the lateral walls this method is unsuitable. Radium element should be employed cystoscopically in preference to radon seeds because the cystoscopic implantation of small platinum needles by the author's method is technically no more difficult than the implantation of radon and on expiration of the allotted time of radiation the needles are removed. Radon usually is left in place and becomes a permanent foreign body, which may be undesirable in the presence of infection, especially in the region of the trigone; in charity services and in indigent patients in private practice the expense of gold radon seeds may be prohibitive. The author treated 11 patients by cystoscopic implantation of radium element. Of the 5 who have died the survival varied between six months and six years. Among the 6 still surviving, some have been treated quite recently. The neoplasms were mostly of grades 2 and 3. The chief indication for irradiation in bladder carcinoma has been advanced age. It is generally agreed that the avoidance of open surgery in such a group is desirable.

Kansas Medical Society Journal, Topeka

45:161-196 (May) 1944

Sternberg and Fort Harker Cholera Epidemic of 1867. J. M. Schneck. —p. 161.
Possible Transmission Factors in Poliomyelitis. O. S. Walters.—p. 163.
Pathologic Physiology of Hypertension. G. A. Walker.—p. 167.

45:197-232 (June) 1944

Management of Acute Infectious Diseases in Childhood. A. L. Hoyne. —p. 197.
Staphylococcus Osteomyelitis: Case Report. F. L. Feireabend.—p. 200.
Sulfathiazole in Gonorrhea. B. M. Marshall.—p. 201.

Military Surgeon, Washington, D. C.

94:325-398 (June) 1944

Sanitary Problems of Tropical Advanced Base. L. W. Johnson.—p. 325.
Orthopedic Surgery in Treatment of Wounds. A. E. Porritt.—p. 335.
Surgery in Desert Warfare. P. B. Ascroft.—p. 337.
*Use of Sulfathiazole as Prophylactic Agent. J. O. Gooch and A. L. Gorby.—p. 339.
Medical Examination at Armed Forces Induction Station: Observations of Medical Examining Physician. F. K. Herpel.—p. 345.
Clinical Review of Schistosomiasis with Presentation of an Interesting Case. R. R. Pliskin.—p. 351.
Vincent's Infection. H. L. Malter.—p. 358.
Radical Operation with Plastic Closure for Cure of Ingrowing Nails. L. C. Bennett.—p. 361.
Clinical Observations on Dengue Fever: Report of 100 Cases. J. S. Diasio and F. MacD. Richardson.—p. 365.
Value of Sedimentation Rate Determinations in Management of Primary Atypical Pneumonia, Etiology Unknown. S. A. Wolfson.—p. 370.
Traction of Soft Tissues: New Method Following Amputation. J. L. Magrath.—p. 373.
Field Device for Hand Washing. H. Greenbaum.—p. 374.

Sulfathiazole Prophylaxis for Gonorrhea.—Gooch and Gorby describe three different plans of sulfathiazole prophylaxis in units with venereal disease rates in excess of 100 per thousand a year. The use of regularly established prophylactic stations (these stations do not administer sulfathiazole) as soon as possible after contact was encouraged, directing that sulfathiazole should be considered as an adjunct to such measures rather than supplanting them. It was emphasized that sulfathiazole in no way protected against syphilis and that syphilis prophylactic measures should not be neglected. At the time the sulfathiazole prophylaxis was put into effect the annual gonorrhea rate of the units affected averaged 170 per thousand. After two and one-half months of application the annual rate was reduced to an average of 70 per thousand. The rate as it now stands is due to cases contracted on furloughs, which often means that the men are away from the organization for fifteen days. They frequently return from furlough with acute gonorrhea. Aside from the method in use with those units exhibiting high venereal disease rates, different methods were used to establish the most efficacious dosage, the smallest effective dose, the proper timing of the dosage and to compare sulfathiazole gonorrhea prophylaxis with the standardized venereal disease prophylactic method using soap, five minute urethral instillation of 2 per cent solution of strong protein silver and ointment of mild mercurous chloride. After describing the prophylaxis used in four different groups the author says that in those using sulfathiazole the drug was entirely administered after the exposure except in group 4. In this group 2 Gm. of sulfathiazole was given as the man left his company area on pass and when he returned, the drug being given before and after exposure. During the period covered by this report there was a reduction in the venereal disease rate from gonorrhea alone from an approximate annual figure of 16 to 11 per thousand. The authors concluded that (1) sulfathiazole is an effective gonor-

rheal prophylactic agent, (2) the average individual prefers the sulfathiazole type of prophylaxis over the urethral instillation method, (3) sulfathiazole gonorrheal prophylaxis is effective for a longer period following exposure, (4) in prophylactic dosage toxicity and sensitivity reactions to the drug are negligible, (5) a total dose of 2 Gm. of sulfathiazole appears as effective as twice that amount, (6) there was a concurrent lowering of the common respiratory disease rate in those units placed on a mandatory sulfathiazole gonorrheal prophylaxis regimen, i. e. those units with high venereal disease rates, and (7) there has been a concurrent lowering of the syphilis rate as a result of increase in the number of prophylactic administrations.

Minnesota Medicine, St. Paul

27:337-432 (May) 1944

Social and Economic Trends in Relation to Medical Practice. W. L. Burnap.—p. 355.
Postwar Planning for Medicine. E. J. Carey.—p. 359.
Treatment of War Wounds of Extremities. C. A. Caspers.—p. 364.
Challenge to Psychiatry in Postwar Period. E. K. Clarke.—p. 367.

27:433-512 (June) 1944

Manpower Problems in Professional Fields. D. Bjornaraa.—p. 453.
Clinical Use of Dicumarol: Report of Cases. E. E. Eckstam.—p. 455.
Hand Infections. R. F. Hedin.—p. 459.
Crippled Appendix—Pediatric Problem. W. R. Shannon.—p. 466.
Isolation from Milk Supplies of Specific Types of Green Producing (Alpha) Streptococci and Their Thermal Death Point in Milk. E. C. Rosenow.—p. 469.

New England Journal of Medicine, Boston

230:685-720 (June 8) 1944

Medical Service in Industry. D. O'Hara.—p. 685.
Clinical Significance of Bacteriuria in Patients with Spinal Cord Injuries. D. Badal, D. Munro and M. E. Lamb.—p. 688.
Tuberculosis of Lower Lobe. E. Z. Ossen.—p. 693.
Parathyroid Glands and Parathormone. A. Pope and J. C. Aub.—p. 698.

230:721-748 (June 15) 1944

Treatment of Anuria. C. W. Styron and W. F. Leadbetter.—p. 721.
Dr. Saul Tchernichovsky, 1875-1943: Hebrew Medical Poet Laureate. H. A. Savitz.—p. 728.
New Biologic Concepts Derived from Research on Sulfonamide Drugs. B. D. Davis.—p. 734.

New Orleans Medical and Surgical Journal

96:551-610 (June) 1944

President's Address: Progress of Medicine and Surgery in United States in Last Fifty Years and What the Future Holds for It Under the Wagner-Murray-Dingell Bill. C. C. deGravelles.—p. 551.
Memorial Address. J. Q. Graves.—p. 556.
Peace and Health. R. Fitz.—p. 557.
*Ephedrine Sulfate in Treatment of Noctural Enuresis. W. E. Kittredge and H. G. Brown.—p. 562.
Adenomya of Gallbladder: Report of Multiple Papillary Adenomyoma in 15 Year Old Boy. G. McHardy and D. Browne.—p. 567.
*Incidence of Peptic Ulcer. M. Patterson.—p. 570.

Ephedrine Sulfate in Nocturnal Enuresis.—Parkhurst suggested in 1930 the use of ephedrine in incontinence of urine. Kittredge and Brown used the drug for the control of enuresis in 25 children who were chronic bed wetters. Twenty-three of these immediately became continent and remained so as long as the drug was administered. It was given in a single dose of ¾ grain (50 mg.) each night at bedtime, and no other measures were taken to influence the bed wetting habit. The drug was continued in each case for two weeks and then withdrawn. It was then noted that enuresis returned in 11 of the 23 children; the other 12 remained well. The 2 who were not influenced were incorrigible children of low mentality. Each case is first carefully studied to eliminate organic pathologic conditions which might cause frequency of urination stimulating enuresis. It is always necessary to eliminate the possibility of infection in the urine, mechanical obstruction to the emptying of the bladder with resultant retention, or neurologic defect which would interfere with normal function of the bladder. The drug is recommended because of its ease of administration, absence of disagreeable reactions and excellent results.

Incidence of Peptic Ulcer.—Patterson states that statistical reports from various countries reveal a manifest variability in the incidence of peptic ulcer from country to country but that in America approximately 12 per cent of all persons have peptic ulcer at some time in their lives. The ratio of gastric to duodenal ulcer is extremely variable, but among patients seen in this country duodenal lesions predominate about 4 to 1. The period of life from the thirtieth to the sixtieth year with a peak in the middle age years (35 to 50) is the most frequent period for peptic ulcer, and duodenal ulcer makes its appearance earlier in life than the gastric ulcer. Peptic ulcer is predominantly a lesion found in the male. This predominance is more obvious in cases of duodenal ulcer than of gastric ulcer. The main evidence, though slight, points toward an endocrine basis. Hemorrhage is the most frequent complication, but perforation is the more serious. Opinions as to the role of occupation in peptic ulcer are contradictory. The impression that the disease is most prevalent among those who lead lives entailing great nervous strain and responsibility awaits proof. Draper's contention that there is a body type peculiar to peptic ulcer is unreliable. Some authors obtained a positive family history in a large percentage of ulcer patients. Peptic ulcer is of importance in the present national crisis. Dyspepsia is the number one medical problem in the armed forces, and reports show that the incidence of ulcer is 30 per cent or over, with the majority in the duodenum. The author thinks that the high incidence of peptic ulcer in the armed forces is not a result of the war but that the war called attention to the numerous cases which existed but were not recognized.

New York State Journal of Medicine, New York

44:1169-1280 (June 1) 1944

Prolonged Intravenous Pentothal Sodium Anesthesia, Especially with Reference to Its Application to Military Surgery. B. A. Greene.—p. 1205.
Inhalation Therapy Using Mineral Waters and Medicated Oils. W. S. McClellan, with technical assistance of Margaret Rogers.—p. 1214.
Antepartum Necrosis of Anterior Lobe of Pituitary Gland. J. S. Taylor and E. F. Shea.—p. 1223.
*Preventive Aspects of Coronary Disease and Myocardial Infarction. M. Plotz.—p. 1227.
Cesarean Section: Advantages and Disadvantages of Present Day Types. J. P. Marr.—p. 1230.

Preventive Aspects of Coronary Disease.—Plotz thinks that preventive measures are possible for a certain number of patients with coronary disease or myocardial infarction. First there is the patient who has already had one attack of coronary thrombosis. Next there is the man with angina pectoris. Next there are middle aged and aged persons with electrocardiographic evidence of heart damage without symptoms. Given certain conditions, their coronary arteries will fail. Somewhat less vulnerable but still requiring special vigilance are patients with hypertension, diabetes, myxedema, polycythemia or elevated blood cholesterol from any cause. Coronary thrombosis practically never occurs in an undamaged artery. It is preceded by an atheroma. Terrifying pain, shock and changes in the cardiogram are only the final act in coronary thrombosis. Preceding this there may be a prodromal stage of precordial pain resembling coronary pain. It is like a prolonged, atypical attack of angina pectoris and is a reflection of reduced coronary circulation and anoxia of the heart. If a patient falls into one of the vulnerable categories such an attack should lead one to suspect an impending coronary thrombosis. A man who suddenly develops angina pectoris for the first time should be put in the same category. These patients should be treated as though they had a cardiac infarction. Bed rest for five to fourteen days and use of papaverine to increase the pulmonary circulation are essential. Patients should be warned against the use of glyceryl trinitrate at this stage. If it does not relieve pain promptly it should not be used again, because the repeated use lowers the blood pressure and increases the possibility of infarction. Sharp and prolonged reduction of blood pressure may be fatal to a patient of the vulnerable classes. Therefore he must be protected against such events as shocking operations, spinal anesthesias, which lower the blood pressure, and severe hemorrhages. In this connection the author cites several illustrative cases and says that for the past two years he has employed slow plasma transfusion for those patients whose systolic blood pressure has fallen below 90. He feels that several lives have been saved by preventing the coronary head pressure from falling too low.

North Carolina Medical Journal, Winston-Salem

5:173-216 (May) 1944

Challenge to the Doctors of North Carolina. J. W. Vernon.—p. 173.
Interstitial Nephritis: Case Report. E. S. Faison.—p. 179.
Streptococcal Disease in Infancy and Childhood. E. V. Turner.—p. 182.
Brucellosis. C. G. Reid.—p. 186.
Management of Occipitoposterior Position. T. L. Lee.—p. 189.
Thumbnail Sketches of Eminent Physicians. J. C. Trent.—p. 193.

5:217-264 (June) 1944

Address of President-Elect: Extension of Medical Care in North Carolina. P. F. Whitaker.—p. 217.
Treatment of War Casualties. W. Walters.—p. 222.
Human Health and Common Weal. J. K. Hall.—p. 227.
Continuous Caudal Analgesia: Report on Its Use in 100 Obstetric Cases. A. T. Thorp.—p. 232.
*Fatal Poisoning with Thiocyanate in Treatment of Hypertension. K. D. Weeks.—p. 234.
Cardiospasm. W. H. Sprunt and J. A. Harill.—p. 238.
Resection of Presacral Nerves in Functional Uterine Dysmenorrhea. J. W. Farthing.—p. 241.

Poisoning with Thiocyanate in Hypertension.—Weeks reports 2 instances of severe potassium thiocyanate intoxication, one in a 41 year old married Negro woman who recovered and the other in a 45 year old white married man whose illness terminated in death. Both patients presented a clinical condition characteristic of severe thiocyanate intoxication in which psychosis, delirium, confusion and signs of central nervous system irritation predominated. The highest blood level obtained from the patient who recovered was 32 mg. per hundred cubic centimeters and in the fatal case it was 36 mg. per hundred cubic centimeters. The latter patient lapsed into coma on the third hospital day and died shortly thereafter. Thiocyanate intoxication was not suspected on admission in either case. An unusual feature of both cases, and one which has been previously reported in only 1 or 2 cases, was the occurrence of unexplained vascular phenomena. The patient who recovered had clinical, physical and x-ray evidence of pulmonary infarction. The explanation of its production was not apparent. In the other case there was found at necropsy a subdural hematoma in the left frontoparietal region which had ruptured into the subarachnoid space. There was no history of head injury before death, and no explanation was found at necropsy. Anginal pain, arterial thrombosis and painful enlargement of the thyroid may also be produced. The high cerebrospinal fluid thiocyanate level found in the 2 cases reported here suggests that signs and symptoms of severe poisoning are primarily due to the toxic effect on the central nervous system. This is substantiated by the absence of significant pathologic changes in other organs.

Northwest Medicine, Seattle

43:129-156 (May) 1944

What the Future Holds for America. C. E. Martin.—p. 132.
Incidence of Common Duct Stones and Postoperative Management of the T-Tube. J. W. Baker and M. H. Evoy.—p. 137.
Human Salmonella Suipestifer Infection: Report of Unusual Case. J. E. Hunter, C. A. Andresen, W. B. Hutchison.—p. 142.
Electrocardiogram After Exercise in Angina Pectoris. G. D. Capaccio.—p. 144.

43:157-184 (June) 1944

Current Problems in Relation to Accelerated Program for Premedical and Medical Education. O. Larsell.—p. 161.
*Filariasis. W. O. Ramey.—p. 164.
Rheumatic Fever in Childhood. P. F. Guy.—p. 166.
Infectious Neuritis. A. L. Severeide.—p. 169.
Hemorrhagic Tumors of Ovary. E. B. Brookbank.—p. 170.
Treatment of Parasites of Small Intestine with Dover's Powder. J. O. George.—p. 172.

Filariasis.—Ramey says that filariasis is primarily the result of fibrotic changes, causing obstruction to the lymphatic and venous flow. Among the microscopic changes are hyperplasia of the connective tissue and infiltration of lymphocytes, basophilic cells and eosinophils. These changes may be manifested as (1) chronic adenitis with or without obstruction and elephantiasis or (2) dilatation of lymphatics with or without elephantiasis. Some other lesions are (1) the lymphatic varix, which is a tumor consisting of a mass of dilated lymph vessels, (2) lymph scrotum, the result of dilatation of the scrotal lymphatic system and pronounced lymphedema, elephantiasis frequently supervening and adding to the enlargement, and (3) elephantoid fever, which is characterized by pyrexia attributable to inflammation of intra-abdominal or intrapelvic structures and is usually associated with pain. The onset of the disease is characterized by pyrexia of 102 to 104 F., headaches, rigor, anorexia, often nausea, occasionally vomiting and a depressed mental state. The affected part presents signs of an acute inflammatory process, which may be of the lymphatic type or the erysipeloid variety; usually the acute symptoms largely subside in a few days, but the pronounced swelling persists. More than 70 per cent of cases recently reported from a mobile hospital showed scrotal involvement and, in more than half of these, involvement of an extremity. Septicemia and death may supervene. The tendency of the fever to recur, the severe rigor, pyrexia and terminal diaphoresis have caused it to be mistaken for malaria. There is no specific drug therapy for filariasis. The treatment should consist of bed rest, morphine for pain, elevation of the affected part to assist in postural drainage, a semielastic bandage to prevent swelling, keeping the skin well cleansed with soap and water, sulfonamide drugs, which frequently are found to exercise a distinctly beneficial effect, and surgical operation for such conditions as lymph scrotum. The only known definite aid to filarial disease is removal to a cool climate; the patient should be told frankly the nature and prognosis of the disease. The author stresses that filariasis may be acquired after only a few weeks stay in an endemic area. The extensive distribution of American forces in areas where filariasis is endemic suggests that filarial infection may be introduced in all parts of the United States. It becomes necessary to include a consideration of filariasis in the differential diagnosis of acute fevers, edema, pseudedema, varicosities, glandular enlargements, lymphatic disease, general enlargements of the extremities, synovitis and arthritis in all persons returning from the tropics and subtropics.

Pennsylvania Medical Journal, Harrisburg

47:769-864 (May) 1944

Medical Progress in War Effort. D. L. Borden.—p. 783.
Surgical Treatment of Cranial Trauma. F. C. Grant.—p. 790.
Etiology and Control of Progressive Axial Myopia. H. H. Turner.—p. 793.
Bromide Intoxication: Some Observations on Its Treatment with Sodium Chloride and Desoxycorticosterone. M. G. Wohl and H. F. Robertson.—p. 802.

47:865-960 (June) 1944

Selection and Interpretation of Laboratory Tests. W. M. Yater.—p. 883.
Typhus Fever: Case Report. R. C. Hamilton and J. C. Fleming.—p. 892.
Trends and Shortcomings in Approach to Gastrointestinal Diseases: Review Based on Experience in an Army General Hospital. J. E. Berk.—p. 897.
Problems of Rural Surgeon. C. M. Hower.—p. 902.

Puerto Rico J. Pub. Health & Trop. Med., San Juan

19:551-698 (June) 1944

Experimental Plague in Guinea Pigs Inoculated with Pasteurella Pestis of Ecuadorian Origin. A. Macchiavello and D. Urigüen.—p. 577.
Use of Calcium Gluconate in Treatment of Malarial Chills. D. S. Stevenson.—p. 602.
Observations on Nocturnal Activity of Anopheles and Certain Other Mosquitoes in Eastern Puerto Rico. A. A. Weathersbee and G. E. Bohart.—p. 626.
Note on Mosquito Distribution Records of Puerto Rico and of Virgin Islands. A. A. Weathersbee.—p. 643.
Comparative Study of Results Obtained from Flocculation and Complement Fixation Tests Carried out Among 3,994 Selectees and Volunteers in 1941. O. Costa Mandry and J. L. Janer.—p. 649.
Note on Treatment of Schistosomiasis Mansoni with Gentian Violet. F. Hernández Morales.—p. 666.

Rocky Mountain Medical Journal, Denver

41:361-448 (June) 1944

Coordination of Industrial Hygiene Instruction with Other Clinical Training. D. E. Cummings.—p. 379.
Tuberculosis and War Industry. W. P. Shepard.—p. 381.
Elements of Diagnosis and Prognosis in Pneumonoconiosis. L. U. Gardner.—p. 385.
Review of Silicosis for Industrial Hygienist and Medical Practitioner. L. E. Hamlin.—p. 391.
Physician's Responsibility in Compensation Law Administration. B. E. Kuechle.—p. 399.
Benzene (Benzol) Poisoning: Report of Fatal Case with Autopsy. Findings. R. H. Ackerly and G. E. Hawlick.—p. 402.
Management of Silicotic Patients. P. J. Ramberger.—p. 405.

Surgery, Gynecology and Obstetrics, Chicago

78:561-662 (June) 1944

Surgical Construction of 80 Cases of Artificial Esophagus. S. S. Yudin. —p. 561.
Cortical Kidney Tumor—Analysis of 100 Consecutive Cases. C. C. Herger and H. R. Sauer.—p. 584.
Surgical Division of Spinothalamic Tract in Medulla. R. D. Adams and D. Munro.—p. 591.
Use of Pectin and Other Agents to Prevent Shock. L. Figueroa and F. J. Lavieri.—p. 600.
Studies in Lymphatics of Female Urinary Bladder. T. O. Powell. —p. 605.
*Rh Factor in Intragroup Blood Transfusion Reactions. B. C. Butler, D. N. Danforth and J. Scudder.—p. 610.
Experimental Head Injury with Special Reference to Certain Chemical Factors in Acute Trauma. E. S. Gurdjian, J. E. Webster and W. E. Stone.—p. 618.
Translocation of Peroneus Longus Tendon for Paralytic Calcaneus Deformity of Foot. W. H. Bickel and J. H. Moe.—p. 627.
*Fractures of Neck of Femur: An Analysis of 157 Intracapsular and Extracapsular Fractures. I. E. Siris and J. D. Ryan.—p. 631.
Induction Examination for Inguinal Hernia. L. Carp.—p. 640.
Mesenteric Pouch Hernia Simulating Paraduodenal Hernia. R. B. McCarty and A. J. Present.—p. 643.
Repair of an Avulsed Scrotum. E. P. Whelan.—p. 649.
Three Pin Method for Treatment of Severely Comminuted Fractures of Os Calcis.—p. 653.

Rh Factor in Intragroup Blood Transfusion Reactions.—Butler and his associates observed an Rh negative obstetric patient who carried a dead fetus for two months and who then at the middle of the seventh month of pregnancy aborted a macerated stillbirth. Following the abortion, because of uncontrollable uterine hemorrhage, the patient went into shock. One hundred cubic centimeters of group O Rh positive blood was administered. A severe hemolytic transfusion reaction occurred which was characterized by chills and fever, hemoglobinuria, jaundice, oliguria and convulsions. The blood chemical findings are tabulated. Ten days after the transfusion reaction the woman had generalized convulsions, but she gradually recovered. The authors selected 25 similar cases of intragroup transfusion reaction from the literature and present them in tabulated chart form. They also outline a rational method of therapy. They emphasize that under no circumstances should obstetric patients be transfused with Rh positive blood unless the patients have been tested for the Rh factor.

Fractures of Neck of Femur.—Siris and Ryan analyze the management of 157 consecutive fractures of the neck and intertrochanteric region of the femur seen in the fracture service of the Third (New York University) Division of Bellevue Hospital from Jan. 1, 1941 to June 30, 1943. They stress that the treatment of choice for the intracapsular fractures in the aged and feeble is the immediate insertion of a Smith-Petersen cannulated three flanged nail or similar device. The treatment of choice for the intertrochanteric fractures in the aged is the immediate insertion of a device incorporating the principle of a Smith-Petersen nail and Hawley bar, preferably a Moore-Blount blade plate. For intertrochanteric fractures in the younger age group bilateral Russell traction suspension has given satisfactory results, and the authors see no reason at present to change their opinion. External pin fixation should not replace internal fixation for fractures of the hip or intertrochanteric region. Other than expediting the procedure of transfixion and minimizing the immediate trauma, it has none of the advantages of internal fixation. It is an extremely hazardous procedure and should be restricted to those who have had experience and are familiar with its technic. The authors think that the patients who are in a poor physical condition on admission have a better chance of survival if they are operated on immediately rather than waiting to see if their general condition improves. They disagree with the selection of survivals policy in which all patients are treated conservatively for a few days and then the operation is decided on only for those who it is expected will survive. Immediate operation permits early ambulation in bed without pain and reduced incidence of potential complications and allows early ambulation with crutches. The use of local anesthesia, focal skin clips and guide wires and the three sets of indispensable roentgenograms to determine (1) the accuracy of reduction and location of the skin clip in relation to the head of the femur, (2) the position of the guide wires and (3) the position of the nail will enhance the ability of the surgeon to expedite the proper insertion of the transfixion device.

Texas State Journal of Medicine, Fort Worth

40:1-42 (May) 1944

Psychosomatic Medicine. J. R. Ewalt.—p. 5.
Preparation of Plasma. J. H. Glynn.—p. 10.
Sulfonamide Treatment of Gas Gangrene. R. L. Sewell.—p. 12.
Gastrointestinal Tuberculosis: Medical Aspects. G. M. Underwood.—p. 14.
Spinal Anesthesia. C. M. Simpson and E. O. Bradfield.—p. 18.
Problems Pertaining to Socialization of Medicine. A. E. Greer.—p. 24.

Virginia Medical Monthly, Richmond

71:279-338 (June) 1944

Preliminary Report of Study of 200 Autopsy Cases at Eastern State Hospital, with Special Emphasis on Neuropathology and Brain Tumor in Old Age. I. S. Zfass and W. Riese.—p. 281.
*Femoral Vein Ligation in the Treatment of Pulmonary Embolism Due to Femoral Thrombophlebitis. E. L. Lowenberg.—p. 288.
*Medical Treatment of Pulmonary Embolism. J. R. Beckwith.—p. 296.
Questions on Vitamin B Complex and on Iodine, Sulfocyanate and Mendelejeff's Law. J. H. Smith.—p. 301.
False Negative Results in Friedman Test for Pregnancy. R. Buxton. —p. 303.
Primary Atypical Pneumonia. S. G. Page Jr. and C. R. Tittle.—p. 305.
Spina Bifida and Polydactyly in One Egg Twins: Case Report and Medical Aspects. W. B. Quisenberry.—p. 309.
Demonstration of Tuberculous Bacillemia: Comparison of Guinea Pig Inoculation of Whole Blood and Sediment Concentrated by Loewenstein Method. J. S. Howe.—p. 312.
George Ben Johnston and Listerism. F. S. Johns.—p. 314.

Femoral Vein Ligation in Pulmonary Embolism.—Lowenberg reports 3 cases of pulmonary embolism in which the femoral vein was ligated, with cessation of the embolic episodes. He also reports 2 cases in which ligation was not performed, with fatal consequences. Emphasizing the importance of early recognition of thrombophlebitis of the lower extremity and especially in the deep veins of the calf, he discusses the importance of Homans' test and the status of venography. He advocates femoral vein ligation as a routine emergency procedure whenever pulmonary embolism incident to lower extremity thrombophlebitis has occurred. In such instances the procedure may well be life saving. Whether femoral vein ligation is to be routinely performed in all cases of deep vein thrombosis remains to be proved, but in time the dictum may well be "the treatment of femoral vein thrombophlebitis is femoral ligation." Ligation of the femoral vein at as high a level as possible often has a salutary effect on the thrombophlebitic process even though the ligation is not performed entirely above the inflammatory process, owing to total interruption of the blood flow through the affected veins.

Medical Treatment of Pulmonary Embolism.—Beckwith shows that the classic picture of pulmonary embolism is not difficult to recognize. When a patient who has been lying in bed sits up or strains at stool and suddenly becomes dyspneic and develops severe substernal pain, pallor, sweating, weak rapid pulse and low blood pressure, the diagnosis is obvious. At times the symptomatology may be bizarre. Pneumonia, pleurisy or progressive heart failure may be suspected. The finding of a hitherto unsuspected thrombosis of a deep leg vein may be a lead. X-ray examination may also be helpful. Characteristic electrocardiographic changes often occur. Careful clinical examination of the patient is very necessary, and detection of signs indicating pulmonary hypertension and right ventricular failure is important. When an acute episode occurs and the diagnosis of pulmonary embolism is made, therapy should be immediately instituted. This should be directed at relieving the anoxemia by the administration of oxygen in high concentration and simultaneously making an effort to reestablish the impaired circulation. The latter can be done by the administration of atropine 1/150 grain (0.0013 Gm.) and papaverine ½ grain (0.032 Gm.) intravenously. Then atropine and papaverine should be given every four hours. The response is often dramatic, and a patient who looks moribund may be "responsive" in a short while. The heart rate becomes slower, blood pressure rises, the heart sounds become louder and the color improves. During the past two years the author has seen 3 cases of pulmonary embolism shortly after the condition occurred. All were treated as described and all obtained dramatic relief following the initial attack. Two died later with subsequent attacks and 1 recovered completely. It is probable that, had the focus of the embolus been found, the latter episodes could have been prevented. The cases are presented.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

19:1-42 (March) 1944

Erythroblastosis Foetalis. J. R. Gilmore.—p. 1.
*Scheme for Prevention of Cross Infection in Children's Wards. N. M. Jacoby.—p. 26.

Prevention of Cross Infection in Children's Wards.—Jacoby describes a scheme which was to guard against the dangers of cross infection and was carried out for a year in a new children's ward. A plan of the ward is shown in a diagram. Infants up to 18 months of age who had no infection were admitted to single rooms where no case of known or suspected infection was ever allowed. Infants up to 18 months of age who, although suffering from an infection which excluded them from class 1, are themselves equally susceptible to cross infection, were likewise admitted to single rooms. Children over the age of 18 months suffering from noninfectious disease, e. g. rheumatic fever, chorea, nephritis, diabetes and epilepsy, were admitted to the larger wardlets (with 4 to 6 beds). Children of all ages suffering from infectious diseases, e. g. tonsillitis, respiratory infection, alimentary infection and otitis media, were admitted to the small wardlets, one type of disease being kept in each wardlets as far as possible. Children of all ages suffering from tuberculosis were admitted to the large ward originally designed as a solarium. Only fully trained nurses or senior probationers were selected for nursing, and as far as possible no nurse was given charge of "clean" and infected cases at the same time. All doctors, nurses, students, cleaners, visitors and any one else who wished to enter a ward was required to wear a gauze mask covering the nose and mouth. Infectious cases were nursed on full barrier precautions. Children who were not continuously in bed were not allowed to leave their rooms. The infants' feeds were prepared with full aseptic technic. No precautions, other than those in general use in the hospital, were taken over the food of the older children. Visitors were discouraged. The best results as regards prevention of cross infection were obtained in groups 1 and 2, who were given the best bed isolation. The highest incidence of cross infection was among the tuberculous children, and this is readily explained by the fact that they occupied the largest ward and stayed in the hospital for very long periods. The total incidence at 6 per cent appears to be of a low order compared with 18.9 per cent reported by Wright in 1940. In the conclusion the author stresses once more the importance of bed isolation, careful classification on admission, a competent nursing staff and face masking. He shows that, if children's wards are to be made safer, attention will have to be paid to their architecture, and the staffing with nurses must be on a generous scale. Moreover, the number of beds for children will have to be increased.

British Heart Journal, London

6:53-114 (April) 1944

Paroxysmal Heart Block and Ventricular Standstill. J. S. Lawrence and G. W. Forbes.—p. 53.
Heart Block with Aneurysm of Aortic Sinus. P. F. Duras.—p. 61.
Stokes-Adams Attacks in Child. V. S. Stern.—p. 66.
*Complete Heart Block. M. Campbell.—p. 69.
Rare Case of Complete Heart Block. K. Saracoglu.—p. 93.
Social and Economic Conditions and Incidence of Rheumatic Heart Disease. G. H. Daniel.—p. 103.
Unusual Electrocardiogram in Dextrocardia. J. M. Holford.—p. 105.
Auriculoventricular Rhythm. R. A. Miller.—p. 107.

Complete Heart Block.—Campbell discusses 64 cases of heart block, mostly complete, which were seen during the same period as 29 cases with dropped beats and 140 cases with latent heart block. Of the patients attending the cardiographic department of Guy's Hospital during twelve years 0.6 per cent had complete, 0.5 per cent partial and 2.2 per cent latent heart block. The author gives particular attention to the prognosis, incidence and significance of Stokes-Adams attacks and the extent to which complete block remains persistent or varies to lower grades of partial or latent block. Complete heart block is most often seen in men in the seventh decade with enlarged hearts and atherosclerosis but no other evidence of gross heart disease. Four fifths of the patients were men and 84 per cent were over 50 years of age. Syphilitic and rheumatic heart disease were responsible for only just over 10 per cent of the cases. Myocardial disease was responsible in three fourths of the cases. Cardiac enlargement with no other signs of atherosclerosis was the evidence of myocardial disease in nearly half of the cases, high blood pressure, angina pectoris or congestive failure being present in the other half. The heart rate averaged just under 35 (excluding congenital cases, in which it was generally 40 to 56). Heart block may be complete, partial, partial with dropped beats or latent. Complete heart block may be established or varying, changing to other degrees of block, or interrupted. It may also be transient, due to a known infection or to a specific episode such as cardiac infarction, or paroxysmal, of which there are two varieties, paroxysmal complete heart block when the usual rhythm is latent heart block and paroxysmal heart block (complete) when the usual rhythm shows a normal PR interval. Although complete heart block is a serious lesion, some, especially those under 40, live for many years in reasonably good health. Of the author's patients 50 were followed for more than two years or until death. Thirty-four were dead after an average period of 2.5 years; others were observed for from two to six years and still others for from seven to twenty years. Stokes-Adams attacks were present in half the patients with complete heart block. When they were present they were one of the earliest if not the first significant symptom of heart block. In those without Stokes-Adams attacks, dyspnea or attacks of faintness or dizziness were the main presenting symptoms. The prognosis was considerably worse in those with Stokes-Adams attacks. Of 30 with Stokes-Adams attacks 24 died during the period of observation, whereas of 20 without Stokes-Adams attacks only 10 died. Sixty-one per cent of those with Stokes-Adams attacks died suddenly and of the others only 1 died suddenly. If when a patient is first seen with complete heart block he has not had a Stokes-Adams attack, the risk of such an attack developing or of his dying suddenly is not great, and with each month that has passed the risk becomes still less.

British Journal of Urology, London

16:1-34 (March) 1944

*Treatment of Arterial Hypertension with Potassium Thiocyanate. J. L. D'Silva and G. Evans.—p. 1.

Potassium Thiocyanate in Arterial Hypertension.—D'Silva and Evans studied the effects of potassium thiocyanate in the treatment of 25 patients with hypertension. During the first week the patients were given three times daily 0.1 Gm. of potassium thiocyanate. At the end of the week, that is, after 2.1 Gm. had been given, the serum thiocyanate content was determined. In some patients the serum concentration was less than 4 mg. per hundred cubic centimeters, in others it was between 4 and 11 and in still others it was over 11, in 1 patient as high as 15. This showed that the requirements of the patients varied greatly and that caution was necessary. The dosage was altered in steps of 0.4 Gm. weekly until a serum level of from 5 to 12 (usually from 7 to 9) mg. per hundred cubic centimeters was obtained. Once the individual patient's requirement of potassium thiocyanate was established in the hospital, the follow-up after discharge from the hospital, with blood thiocyanate estimations at less frequent intervals, was fairly satisfactory. Summarizing their observations, the authors say that 11 of the 25 patients responded by a considerable fall and 6 by a slight fall in blood pressure. In 8 cases the blood pressure was unchanged. Headache, vertigo and lack of concentration were the associated symptoms most often relieved. The drug was administered safely to elderly patients and those with electrocardiographic evidence of myocardial degeneration. Two patients with cerebral arteriosclerosis benefited greatly by treatment. No patient with severe renal dysfunction was encountered in this series. Two patients were poisoned with the drug but made uneventful recoveries when its administration was suspended.

Irish Journal of Medical Science, Dublin

6:169-200 (June) 1944

*Heart in Pregnancy, with Special Reference to Public Health. G. E. Donovan.—p. 169.
Middle Meningeal Hemorrhage and Concussion. A. A. McConnell. —p. 179.
Estimation of Promin in Blood and Urine and Study of Its Excretion. A. E. A. Werner.—p. 189.
Observations on Treatment of Psychosis by Electrically Induced Convulsions. J. Delany and J. R. Shea.—p. 193.
Carcinoma of Fallopian Tube. R. M. Corbet.—p. 196.

Heart in Pregnancy.—Donovan points out that the effects of pregnancy on the normal woman may produce both symptoms and signs which closely simulate heart disease, e. g shortness of breath, palpitation, fulness of the neck veins, rales at the lung bases and a change in the radiographic silhouette of the heart similar to that of mitral stenosis. Citing figures mostly of American investigators, Donovan shows that heart disease is not a common complication of pregnancy. He cites a New York report which indicates that in mothers with known heart disease the death rate was 10.3 per thousand pregnancies, compared with 2.0 per thousand for all obstetric patients. Postmortem studies by Glasgow authors revealed that of 813 patients who succumbed during pregnancy or puerperium 108 had acute or chronic heart lesions. Mitral stenosis is the predominant lesion in heart disease complicated by pregnancy. Auricular fibrillation causes approximately four times more deaths than any of the others. Antepartum supervision, with early hospitalization in those cases needing it, materially reduces the mortality rate. There are two schools of thought regarding the best methods of delivery. One favors cesarean section; the other prefers delivery by the natural route with general anesthesia and the application of forceps at a certain stage. Those who prefer cesarean section argue that it is possible to choose a time for the operation with a strict regard for the heart condition of the patient; physical strain of labor is avoided, and there is reasonable certainty of producing a living child. Those who favor natural delivery maintain that women with heart disease usually have easy labors, owing possibly to the laxity of the tissues. The sudden flooding of the circulation at the time of the contraction of the uterus may be a causal factor in the increased incidence of heart failure in the first twenty-four hours of the puerperium. Venous section and the application of a tight abdominal binder as soon as the uterus is evacuated may help. The danger involved in anesthetizing and operating on pregnant women suffering from heart disease has been exaggerated. Probably nitrous oxide and oxygen supplemented by ether is as good as any anesthetic. The use of spinal anesthesia is of doubtful wisdom. It is inadvisable for patients who suffer or have suffered from heart failure to become pregnant. Antepartum clinics should have facilities for special investigations; x-rays and electrocardiographs should be available. Some antepartum cases require hospital treatment, investigation or supervision.

Lancet, London

1:649-680 (May 20) 1944

Reflections on Reform in Medical Education. T. Lewis.—p. 649.
War Surgery of Extremities in Light of Recent Experience. J. Trueta. —p. 651.
Case Finding by Mass Radiography: Report on 500 Selected Cases. A. Kahan and H. G. Close.—p. 653.
*Pneumococcal Meningitis Treated with Penicillin. H. Cairns, E. S. Duthie, W. S. Lewin and H. V. Smith.—p. 655.
Fractured Femoral Shaft: New Approach to Problem. G. R. Fisk. —p. 659.

1:681-712 (May 27) 1944

Gunshot Wounds of Knee Joint. S. J. D. Buxton.—p. 681.
Reflections on Reform in Medical Education. T. Lewis.—p. 685.
Effect of Vitamin C Deficiency on Experimental Wounds: Tensile Strength and Histology. G. H. Bourne.—p. 688.
Pruritus Ani: Practical Approach. A. J. Cantor.—p. 692.
Tissue Culture of Malaria Parasites (Plasmodium Gallinaceum). F. Hawking.—p. 693.

Pneumococcic Meningitis Treated with Penicillin.—Cairns and his co-workers report 8 cases of pneumococcic meningitis treated with intrathecal penicillin, supplemented in 3 cases with penicillin intramuscularly. In 6 cases recovery was complete; in 2 cases leptomeningitis was controlled but death subsequently occurred, one from subdural abscess, the other from brain abscess, ventriculitis and obstruction of the aqueduct of Sylvius. Both sodium and calcium salts have been used intrathecally. Concentrated solutions of approximately 5,000 units per cubic centimeter were made in distilled water, which after Seitz filtration and assay were diluted in water or isotonic solution of sodium chloride to 250 to 500 units per cubic centimeter. Repeated daily injections of these solutions into the lateral ventricles or lumbar subarachnoid space in amounts of 4 to 10 cc. have not produced impairment of nervous function. The usual dosage was 3,000 to 4,000 units per injection. This was given daily for from four to nine days in the uncomplicated cases. The dose was varied: the smallest, 650 units, caused only temporary disappearance of pneumococci; the largest, 20,000 units, was too high for this preparation and produced a severe reaction. The total amount injected intrathecally has varied between 10,000 and 85,000 units. In the mild cases the intrathecal injections of penicillin can all be given by the lumbar route, but the ventricular route should be employed if there is not prompt clinical improvement or if blockage of the cerebrospinal pathways is suspected. In severe cases it would seem desirable to combine lumbar and ventricular injection. When adequate supplies of penicillin become available it may be wise to given penicillin intramuscularly or intravenously for a few days. The authors treated 8 further cases, in 2 of which death occurred. This makes a total of 16 fully treated cases, with 12 recoveries. The majority of the recent cases provided additional evidence of the beneficial effect of sulfonamides. Although much less effective than penicillin sulfonamides can be administered by mouth, and they pass readily from the blood stream into the cerebrospinal fluid.

Medical Journal of Australia, Sydney

1:429-452 (May 13) 1944

Strongyloidiasis in Man: Infestation with Strongyloides Stercoralis (Bavay, 1876). T. E. Lowe and H. O. Lancaster.—p. 429.
Therapeutic Value of Sulfaguanidine in Treatment of Bacillary Dysentery at an Australian General Hospital. B. A. Baker.—p. 435.
Use of Chorioallantois of Developing Chick Embryo in Diagnosis of Smallpox. E. A. North, J. A. Broben and A. H. Mengoni.—p. 437.
Lepromin Test in Laboratory Animals. J. W. Fielding.—p. 439.

Practitioner, London

152:345-408 (June) 1944

Water Metabolism in Relation to Hot Weather. J. M. O'Connor. —p. 345.
Summer Sports. A. Abrahams.—p. 352.
Public Health Aspects of Diseases Prevalent in Warmer Weather. E. H. R. Smithard.—p. 355.
Skin Disorders of Warmer Weather. J. Sommerville.—p. 362.
Diet in Hot Weather. Rose M. Simmonds.—p. 370.
Significance of Minor Head Injuries. G. C. Knight.—p. 377.
Some Problems of Breast Feeding. F. Charlotte Naish.—p. 384.
Interpretation of Physical Signs: VI. In Gynecology. V. B. Green-Armytage.—p. 392.

Schweizerische medizinische Wochenschrift, Basel

73:937-960 (July 31) 1943. **Partial Index**

Organization of Climatic Treatment of Patients Not Suffering from Tuberculosis. K. von Neergaard.—p. 937.
Problems and Requirements of Balneologic and Climatologic Investigations in Switzerland. W. Mörikofer.—p. 939.
Development of Spas in Switzerland; Demands and Requests by Balneologists. J. Weber.—p. 941.
New Methods and Possibilities of Analyses of Springs. W. D. Treadwell.—p. 944.
Spontaneous Sciatic Causalgia. C. Julliard.—p. 946.
*Endocrine Obesity and Spastic Abdominal Syndrome. H. J. Schmidt. —p. 948.
Percutaneous Electrosurgical Puncturing of Lateral Ligament of Knee Joint. F. Becker.—p. 950.
Severe Stenotic Laryngotracheobronchitis Complicated by Pericarditis and Its Effective Treatment by Tracheotomy, Naphazoline Preparation and Sulfathiazole. H. Martin and J. Mury.—p. 951.

Endocrine Obesity and Spastic Abdominal Syndrome.—The subjects of Schmidt's report were 3 women, 29, 44 and 46 years of age with endocrine adiposis associated with a predominant spastic abdominal syndrome. Froehlich's type of hypophysial-genital adiposis was present in 1 case and hypophysial-adrenal obesity associated with pronounced virilism in the 2 others. The spastic abdominal syndrome corresponded to the picture of spastic neuropathic colitis. Renal and ureteral colics in addition to intestinal colics were predominant. They are considered to be manifestations of the same functional dis-

order in two closely related organic systems rather than disorders which are different in principle. Anatomic changes could not be demonstrated in the intestinal canal, but mild bilateral hydronephrosis was shown by 2 of the cases. This hydronephrosis may have been a sequel of the ureteral colics rather than their origin, since a mechanical cause was missing and hydronephrotic changes could not be demonstrated on roentgenologic and postmortem examination. Primary functional disturbances of intestine and ureter in the sense of neuromuscular dyskinesia on a vegetative-nervous base are suggested. Psychic anomaly was present in all 3 cases. A basic depressive attitude was manifested and was associated with a pronounced hysteriform tendency. The accompanying polyneurotic syndrome was characterized by subjective complaints without any objective neurologic findings. The porphyria examination always was negative. The conformity of the symptom complex of these 3 cases suggests an internal genetic relationship, but no indication was presented with regard to its type.

Medicina Española, Valencia

7:277-398 (March) 1944. **Partial Index**

*Early Rising and Pulmonary Embolism After Abdominal Operations. E. Marescot.—p. 284.
Renal Diabetes in Infant: Case. D. Duran.—p. 335.
Vitamin B1 in Therapy of Whooping Cough. L. Cortés de los Reyes.—p. 347.

Early Rising and Pulmonary Embolism.—Marescot emphasizes the importance of early rising after abdominal operations in prevention of pulmonary embolism. The author performed 1,192 abdominal operations during a period of five years in the Pontevedra Hospital. Early rising was practiced in the majority of the cases. Of the small group of patients who remained in bed for more than one week after the operation thrombophlebitis occurred in 4. The patients were ordered to rise immediately from bed, to move their legs and to walk. Phlebitis was controlled. Pulmonary embolism occurred in 1 case. It was benign and controllable.

Revista de la Asoc. Méd. Argentina, Buenos Aires

58:163-216 (April 15) 1944. **Partial Index**

Vitamin K in Therapy of Hypertension. A. Barcellos Ferreyra.—p. 163.
*Dissecting Aneurysm of Aorta with Diagnosis During Life of Patient. J. E. Israel and J. Valotta.—p. 174.
*Adrenal Cortex Extract in Vomiting of Pregnancy. E. Bottiroli.—p. 181.

Dissecting Aneurysm of Aorta.—According to Israel and Valotta, diagnosis of dissecting aneurysm of the aorta during the patient's life is difficult. Changes in the tunica media of the artery constitute the main pathogenic factor. Fissure of the intima layer of the artery and arterial hypertension are inconstant secondary factors. Sudden acute precordial pain which radiates to the back and to the lumbosacral region along the course of the aorta, combined with the feeling of impending death, followed by shock, paralysis and signs of arterial obstruction are the predominant symptoms. X-ray examination shows great enlargement of the thoracic segment of the aortic shadow, double border of the aortic shadow in the frontal view and left ventricular hypertrophy. Recovery after the acute attack is extremely rare, although possible. The authors report that a man aged 43 with hypertension of long standing suffered an acute attack of severe precordial pain followed by paralysis of both legs. The roentgenogram was typical of a dissecting aneurysm of the aorta. Treatment consisted of intravenous injections of papaverine and bed rest. Paralysis greatly improved, the patient being able to walk one month after the attack. He led a comfortable existence for eight months, when he suddenly died. A necropsy was not permitted.

Adrenal Cortex Extract in Vomiting of Pregnancy.—Bottiroli administered adrenal cortex extract to a large number of patients during the last three years for vomiting of pregnancy. The patients belonged to four groups: (1) those with nausea but no vomiting, acidosis or asthenia, (2) patients with acute nausea, vomiting and asthenia but without acidosis, (3) patients with acute nausea, vomiting, asthenia and acidosis and (4) patients with intractable vomiting. Intravenous injections of dextrose solution, a diet of thirst and hunger, enemas of urine of pregnant women, large doses of sodium bicarbonate, insulin, belladonna and thyroid preparations failed in all of the cases. Intramuscular injections of desoxycorticosterone and adrenal cortex extract controlled the nausea and vomiting within three days or a week. It is advisable to administer tablets of 0.10 Gm. of powder of the cortex for one week after vomiting has been controlled. Adrenal cortex extract is a harmless substance which has no contraindications.

Deutsche medizinische Wochenschrift, Leipzig

69:349-378 (April 30) 1943. **Partial Index**

*Constrictive Pericarditis and Its Therapy. F. Koch.—p. 349.
Localization of Urticarial Rash Following Injection of Foreign Serum. A. Cimbal.—p. 353.
Febris Neuralgica Periodica (Wolhynic Fever, Five Days Fever). E. von Bormann.—p. 356.
Allergy in Trichinosis. F. Linneweh and Harmsen.—p. 359.
Thrombopenia and Blood Coagulation. H. Werner.—p. 363.
Gastroenterogenous Pellagra. W. Seitz.—p. 365.
Generalized Thrombopenia After Single Arsphenamine Injection (comment on an article on same subject by Heinsen and Wachter). K. Zieler.—p. 368.
Generalized Thrombopenia After Single Arsphenamine Injection. H. A. Heinsen.—p. 369.

Constrictive Pericarditis and Its Therapy.—The concept of cardiac insufficiency resulting from embarrassment of the diastolic phase of the heart action will be of considerable help in the diagnosis of constrictive pericarditis and as an indication for surgical intervention. Differentiation between tuberculous and rheumatic nature of the condition is of no importance, so far as intervention is concerned, except where definite tuberculous changes in other organs are present, when the operation should not be performed. The earlier the intervention is performed, the more promising the result. Operation gives best results where a complete cure from acute pericarditis has occurred. In such cases even the removal of the feltlike fibrous tissue over the auricles and between the large vessels may be possible and the formation of adhesions with proliferation of connective tissue and cicatrization may be prevented. Operation is recommended nevertheless for the very grave cases, since they are not amenable to any other type of treatment. It is important to commence the surgical intervention on the left ventricle in order that an increased cardiac output may be coped with. Definite improvement may result from this conduct of the operation when first the left ventricle and the right ventricle and even portions of the auricles are freed. Unsatisfactory results, in spite of the fact that the heart had been freed to a large extent, may be due to the anatomic conditions of the posterior wall of the pericardium and its junction with numerous vessels. Adhesions may be particularly pronounced at this area. Two conditions throw light on this state before the intervention. Pulmonary stasis at the base of the lungs, as demonstrated on roentgenologic examination and not amenable to conservative treatment of the heart, is to be regarded as a sequel to the massive obstruction to the filling power of the left auricle. The electrocardiographic recordings of 7 of 20 patients with definite constrictive pericarditis revealed auricular fibrillation, and a peculiar change of the P deflection was shown by the electrocardiograms of the other 13 patients. It was interpreted as a transitional change from the normal stimulation period to fibrillation and as an impairment of the auricular contraction. That corresponds with the anatomic condition of some of these cases, in which calcification was demonstrated on roentgenologic examination. The electrocardiogram of 13 of the 20 cases also showed a definite change in the ST segment, which was depressed more or less below the zero line, particularly in leads 2 and 3. There was an upward convexity of the ST segment ending with a negative T. The peculiar change of the P deflection associated with the well defined changes of the ST segment strongly suggests the occurrence of constrictive pericarditis. In these cases the success of surgical intervention is doubtful and a two stage operation is suggested in those in which the parietal layer and the visceral pericardium can be separated. Conservative management with digitalis, rest, diet and systematic training of the functional capacity of the heart is advisable during the period of improvement following the first stage operation. The second operation is easier and will make more promising the freeing of the right ventricle and of the auricles.

Book Notices

Heart Disease: An Elementary Reference for Physicians. By Robert S. Berghoff, M.D., F.A.C.P., Clinical Professor of Medicine, Loyola University School of Medicine, Chicago. Issued Under the Auspices of the Post-Graduate Committee of the Illinois State Medical Society. State of Illinois, Department of Public Health, Circular No. 176. Paper. Pp. 63. Springfield, 1944.

This booklet has been prepared as an elementary syllabus on heart disease for physicians. There are nine chapters of from three to fourteen pages, on congenital heart disease, rheumatic endocarditis, syphilitic heart disease, arteriosclerotic heart disease, acute and subacute bacterial endocarditis, hypertensive and thyroid heart disease, diseases of the pericardium, abnormalities of rate and rhythm and left ventricular failure vs. right ventricular failure. The plan is excellent but the execution is disappointing. The book fails to present the newest advances in our knowledge of various conditions, such as congenital heart disease in the case of the auricular septal defect. In the discussion of rheumatic heart disease there is little or no statement of the myocardial involvement which is predominant in the early cases and which is responsible for the early dilatation and murmurs. Valvular deformity is a later manifestation. Syphilitic heart disease is essentially syphilitic aortitis and in many cases does not show heart involvement at all. "Heart involvement" should really be "aortic involvement." It is impossible to diagnose syphilitic aortitis early in its course. The symptoms and signs described are late, and it should be emphasized that percussion is notoriously inaccurate in the measurement of the aorta.

Under the heading arteriosclerotic heart disease many cardiologists would doubt any common existence of the senile heart per se, in persons in the fifties, for example. Also individuals vary much in their aging. It is important to recognize that coronary disease is not necessarily a disease of senility; it increases with age, of course, but it is an important disease of youth. Angina pectoris is not necessarily severe. Its position, character and causation are much more important than its severity. Minor myocardial infarction does not require eight weeks for adequate cicatrization, at least for consideration in treatment clinically. Four to six weeks suffice for adequate scar formation. Also it is important to note that the status anginosus, as in the case of acute myocardial infarction and angina pectoris decubitus, is not a chronic state. It should be regarded as an acute or subacute type of heart disease.

In the discussion of subacute bacterial endocarditis, some mention should be made of the reduction of mortality that has already occurred by the use of the sulfonamides and penicillin. In the discussion of hypertensive and thyroid heart disease pulsus alternans is inserted after gallop rhythm as a synonym, but these two conditions are not synonymous. Also most doctors would consider tobacco contraindicated in hypertension, since it is known that most persons show an elevation of blood pressure, especially if they are already hypertensive, during and immediately after smoking. In the chapter on diseases of the pericardium, the important condition of chronic constrictive pericarditis has been omitted. In chapter 8 digitalis intoxication as an important cause of paroxysmal ventricular tachycardia should be included. In the final chapter on congestive failure, one cannot separate, so clearly as is done here, either the symptoms or the treatment of left and right ventricular failure. Cyanosis due to pulmonary congestion is the result of left ventricular failure, not of right, but there may be added cyanosis in right ventricular failure due to stasis in the peripheral circulation. Pain of aortic origin or otherwise is not a characteristic symptom of left ventricular failure, and clubbed fingers are not characteristic of right ventricular failure. Finally, diuretics are important in the treatment of left ventricular failure as well as of right as is also a decreased fluid intake, and it should be noted that digitalis often helps left ventricular failure strikingly.

The usefulness of this pamphlet would be greatly increased with revision to bring it up to date. There are quite a few simple typographic errors that need correction.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1943, With the Comments That Have Appeared in the Journal. Reprinted from The Journal of the American Medical Association. Cloth. Price, $1. Pp. 150. Chicago: American Medical Association, 1944.

In the introduction to its "Official Rules," which have been used as a model by subsequent similar organizations, the Council on Pharmacy and Chemistry states that these were adopted "primarily with the object of protecting the medical profession and the public against fraud, undesirable secrecy and objectionable advertising in connection with proprietary medicinal articles." Later it is stated that the function of the Council is also "to advise the medical profession concerning the status of medicinal articles, . . . to publish reports on claimed advances in the use of drugs and to elaborate standards for the control and identity of drugs that are introduced into materia medica." In its earlier years the Council was chiefly occupied with examining individual preparations for compliance with the Rules, and the early reprints of the Council's reports are predominantly statements concerning the nonacceptability of many preparations. Latterly the emphasis has significantly changed to the more educational phase of the Council's work. The present volume of reprints is an excellent example of this trend. It contains only eight reports on rejected articles; and it is noteworthy that objections to these are on a much higher plane than those it was necessary to urge against the flagrantly quackish preparations of earlier days.

Perhaps the most noteworthy of the nineteen educational reports in this volume is the one declaring the Council's intention of using henceforth only the metric or centimeter-gram-second system in its publications. The report itself gives some interesting and readable history on the subject of weights and measures. Of most timely interest to the general physician as well as to the endocrine specialist is the report on nomenclature of endocrine preparations. The report gives a currently quite complete list of the available commercial preparations, including those not accepted by the Council as well as those which stand accepted. Another report in the field of endocrinology is that recognizing the use of estrogens in the treatment of prostatic carcinoma.

Attention should be called to at least two of the reports concerned with vitamin preparations, namely the status report giving the Council's decision that the evidence does not yet warrant the acceptance of cod liver oil preparations for external use and the report announcing the Council's recognition of the use of massive doses of vitamin D in the treatment of refractory rickets. The Council has previously objected to the use of massive doses of vitamin D in arthritis and in this volume includes a current comment from THE JOURNAL titled "Hope (false) for the Victims of Arthritis," which reemphasizes this objection.

The status report on xanthine compounds gives a much needed delimitation of the therapeutic claims that may be recognized for aminophylline and its related xanthine derivatives. Of similar interest is the report on the local use of sulfonamides in dermatology, and in the same category may be mentioned the report on agents for the treatment of trichomonas vaginitis, which points out that the present aim should not be for new medicaments in this field but for further information, especially concerning failures with those that have been used. In another status report the Council sets forth its conclusion that present evidence does not justify claims for advantage of oral use of sodium sulfonamides over the free drug.

In line with its decision to consider for acceptance various contraceptive preparations, the Council published a status report on conception control, which is included in this volume. The report comprises a series of concise statements on the various preparations and methods of control, prepared by Dr. Robert Latou Dickinson, together with a statement of criteria by which the Council will consider the acceptability of contraceptive jellies, creams and syringe applicators and nozzles, diaphragms and caps.

It cannot be too often said that this volume, as well as the other publications of the Council, remains of paramount interest to all who are concerned with rational use of therapeutic agents.

Taken all together, the printed record of the Council's work represents a fitting monument to a service born of unselfish altruism and continued in a spirit of finest devotion to the best interests of the medical profession and the public.

The Diet Therapy of Disease: A Handbook of Practical Nutrition. By Louis Pelner, M.D., Assistant Attending Physician, Long Island College Hospital, Greenpoint Hospital, and Brooklyn Cancer Institute. Cloth. Price, $3.75. Pp. 143, with 6 illustrations. New York: Personal Diet Service, 1944.

This book is intended for the guidance of the physician in providing the greatest possible benefits to the patient from use of properly selected diets. In many cases there is no therapeutic effect to be derived from the most careful selection of food types, but in such cases proper selection at least can be of value in lightening the burdens of the body.

In the brief introductory discussion covering the basic facts of nutrition, new developments of practical significance in this field are touched on. A question might be raised concerning the classification of vitamins given here as Council accepted and not accepted. A clearer understanding of their status would probably result from their differentiation as those whose significance in human nutrition is now established and those whose relationship to human nutrition is not yet determined.

The body of the book consists of diet lists for some thirty disease conditions in their various forms as well as many types of special diets. For each a sample diet covering the meals of one day is accompanied by a helpful discussion of the fundamental pathology of the disease and the principles governing a diet for that condition. In some cases it is felt that the author attemps to cover too much ground for a book of this nature by going into the differential diagnosis of the disease state. The dietary principles set forth are based on sound, up to date scientific information with numerous references quoted. The actual diet lists are quite simple and apparently have proved themselves practical from long experience. As brought together in one book such as this, a ready reference and sample diet source is available to the medical practitioner for the application of the developments in the science of nutrition.

Fundamentals of Psychiatry. By Edward A. Strecker, M.D., Sc.D., F.A.C.P., Professor of Psychiatry and Chairman of the Department, Undergraduate School of Medicine, University of Pennsylvania, Philadelphia. Second edition. Cloth. Price, $3. Pp. 219, with 15 illustrations. Philadelphia, London & Montreal: J. B. Lippincott Company, 1944.

This book was first published in October 1942. Additional material was added in March 1943, and the present edition includes a single six page chapter on war neuroses that was not in the reprinting of the first edition. Otherwise the book appears to be unchanged except for minor typographic errors. The addition of this brief chapter would hardly seem to justify, in the opinion of the reviewer, a second edition. The book itself is excellent, as was pointed out in a review when it was first issued. Written by one of the leading psychiatrists in America, it is a brief, sound, compressed work, highly readable and excellent for the general medical adviser, who so often is faced with the problems of mental disease. This small manual can again be highly recommended as a useful and accurate summary of present day psychiatry.

Cancer: A Study for Laymen. Prepared for the Women's Field Army of the American Society for the Control of Cancer, Inc. [Compiled by] Clarence C. Little, Sc.D., Managing Director. Paper. Gratis. Pp. 122, with 54 illustrations. New York & Toronto: Farrar & Rinehart, Inc., 1944.

This can be regarded as an excellent manual if one keeps in mind that it is designed for the use of interested lay persons who have time to devote to study and to work in the cause of cancer control. It should not, however, be used outside the circles of interested workers. Its greatest usefulness will be among those who have at least a rudimentary knowledge of biologic science. It is prepared for the Women's Field Army of the American Society for the Control of Cancer, Inc., and is distributed free by that society, which may be addressed at 350 Madison Avenue, New York 17.

Our American Babies: The Art of Baby Care. By Dorothy V. Whipple, M.D. Introduction by C. Anderson Aldrich, M.D. Cloth. Price, $2.50. Pp. 367, with illustrations. New York: M. Barrows and Company, Inc., 1944.

This book is well organized and the material is completely integrated, from antepartum management through the first two years of life. The information given is what every young mother desires and is especially adapted for those who are working. There is a certain authority which comes only from one who has both practical as well as the scientific knowledge of the many problems one encounters in the care of infants. The information on most subjects is very adequate. The chapter on the development of habits and their treatment is delightfully covered and would save much valuable time of the pediatrician if all mothers could read it. The book would make a valuable reference for all persons interested in the care of infants.

One Hundred Years of American Psychiatry. J. K. Hall, M.D., General Editor, Gregory Zilboorg, M.D., Associate Editor, and Henry Alden Bunker, M.D., Assistant Editor. Cloth. Price, $6. Pp. 649, with illustrations. New York: Published for the American Psychiatric Association by Columbia University Press; London: Oxford University Press, 1944.

Psychiatry, like other branches of medicine, has made enormous progress in the last century. In this field American psychiatrists have played an increasingly important part. This volume is not intended to list past achievements or to present a symposium on what American psychiatry is doing today but rather, as pointed out in the foreword, is intended as a historical synthesis of a century of American psychiatric evolution. It is a little surprising to find such extremely wide margins and other wasted space in a book published in these days of paper shortage. The editorial board and the contributors have been well chosen and deserve congratulations on the interesting chapters presented.

Summary of State Legislation Requiring Premarital and Prenatal Examinations for Venereal Diseases. By Aneta E. Bowden, M.A., Ph.D., and George Gould, M.A., LL.B., Assistant Director, Division of Legal and Protective Services, American Social Hygiene Association, New York. Published and distributed by the American Social Hygiene Association in cooperation with United States Public Health Service. Second edition revised by George Gould. Paper. Price, 25 cents. Pp. 30, with 2 illustrations. New York, 1944.

As of Jan. 1, 1944 thirty states had passed legislation to prevent the spread of venereal disease through marriage by requiring a premarital examination as a condition to the issuance of a marriage license. A similar number of states had enacted antepartum examination laws to prevent syphilis in the unborn child. This summary represents an adequate, dependable analysis of such laws which will serve as a practical guide to health authorities, officials issuing marriage licenses, physicians and all others concerned. It will be particularly valuable to those who may be interested in the promotion of similar legislation in states in which laws of this character do not yet exist.

The Management of Neurosyphilis. By Bernhard Dattner, M.D., Jur.D., Associate Clinical Professor of Neurology, New York University Medical College. With the collaboration of Evan W. Thomas, M.D., Assistant Professor of Medicine and Assistant Professor of Dermatology and Syphilology, New York University Medical College, and Gertrude Wexler, M.D., Instructor in Dermatology and Syphilology, New York University Medical College. Foreword by Joseph Earle Moore, M.D., Associate Professor of Medicine and Adjunct Professor of Public Health Administration, Johns Hopkins University, Baltimore. Cloth. Price, $5.50. Pp. 398, with 7 illustrations. New York: Grune & Stratton, 1944.

This book is a practical and much needed contribution. The author published another book on modern treatment of neurosyphilis eleven years ago when he practiced in Vienna. This publication is written along the same lines. It is divided into two parts, namely technics of withdrawal and examination of spinal fluid and methods of treatment, and application and results. The part on the spinal fluid is extremely well written, concise and encyclopedic in nature. It is the best the reviewer has ever seen on the subject. The second part is a textbook in itself. Every known form of treatment is described with technic and results. This book must be purchased by any medical man who treats any form of syphilis. It is the best at the present time. There is an index of authors and subjects.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

EVACUATION OF STOMACH OF INFANTS

To the Editor:—Can you suggest a dependable, safe and quick acting emetic to be used for young infants; one that may be given by mouth or by needle or both? It often happens that children get poisoned on fuel oil and the like, and emptying the stomach with a stomach tube is not altogether satisfactory because of food blocking the outlet of the tube. Syrup of ipecac, I have found, is too slow and cannot be relied on for prompt results.

C. C. Horton, M.D., Pendleton, S. C.

ANSWER.—Emetics are not as commonly used as in former times, though the list of these remedies has remained for the most part unchanged through the years. The emetics which are in common use may be briefly enumerated: Ipecac is used in the form of powder, 1 teaspoon to a glass of water or 1 tablespoon of the syrup in water repeated every fifteen minutes until vomiting is produced. Ipecac is uncertain and in large doses acts as a depressant. Zinc sulfate and copper sulfate are no longer in common use. One-half teaspoon of the zinc salt in water will usually cause emesis. Copper sulfate in 5 grain (0.32 Gm.) doses in warm water repeated in fifteen minutes will cause vomiting with only slight constitutional symptoms, but if not promptly ejected it may cause corrosion of the mucous surfaces. Mustard is safe but not certain in the desired action. One teaspoon in a cup of warm water should be given, repeated every fifteen minutes until vomiting is produced. Salt water, 2 tablespoons to a glass of water, sometimes produces the desired result. Apomorphine is a rapidly acting emetic, though most physicians are reluctant to use it for young infants on account of its toxic and depressant action. For young infants the dose is $\frac{1}{60}$ grain (0.0011 Gm.) hypodermically or $\frac{1}{12}$ to $\frac{1}{20}$ grain (0.0054 to 0.0032 Gm.) by mouth.

The emetics may be employed if lavage is contraindicated or inadvisable, though as a rule they are less reliable and are likely to be more depressing. Lavage is the method of choice in removing poisonous substances from the stomach. A catheter will serve the purpose, the diameter of which should vary with the size of the child. A small funnel may be attached to the lumen of the tube, and the stomach washing may proceed in the usual manner. In most cases it is preferable to attach a 20 cc. glass syringe (larger size if available) to the catheter. Water should be slowly and gently forced through the catheter into the stomach, followed by immediate aspiration. This washing and aspirating process should be frequently repeated until the wash water is clear and free from ingested poison. By use of the syringe the catheter is less likely to be blocked by food substances. If the poison has caused erosion of the mouth, pharynx or digestive tract the passage of a tube is contraindicated. In washing the stomach great care should be taken that food particles and poisonous substances are not aspirated from the pharynx into the lungs. It has been suggested that this accident may occur when the stomach is evacuated in kerosene poisoning, causing pneumonia; others think that if the oil remains long in the stomach it may be absorbed and partially eliminated through the respiratory organs, causing irritation and inflammation in these areas.

CONTRACTURE OF HAND AND MERCURIC CYANIDE DRESSING

To the Editor:—Can a solution of mercuric cyanide used as a wet dressing on an aluminum metacarpal splint cause a permanent deformity of the hand? I have a case in which mercuric cyanide was used as a wet dressing on an aluminum metacarpal splint for an infected hand. Later (within a few weeks) contracture of the hand developed, and now the patient is unable to close his hand completely. He was told by another physician that the cyanide solution caused the deformity. I should like to know if it is possible for the mercuric cyanide to react with the aluminum and produce the contracture of the hand that is now present.

M.D., North Carolina.

ANSWER.—There is no definite information which would permit an answer to this question. It seems extremely doubtful that a combination of mercuric cyanide as a wet dressing with an aluminum splint could be responsible for the injury. Why one should use a destructive chemical like mercuric cyanide in the treatment of a hand infection is difficult to determine.

STRYCHNINE SULFATE FOR NERVOUS MANIFESTATIONS OF ALCOHOLISM

To the Editor:—A colleague recently expressed himself in favor of strychnine sulfate for cases of delirium tremens and acute alcoholic delirium. The thesis of antagonism (chemical or physiologic) between alcohol and strychnine seems to me particularly untenable as a basis for therapy since a patient with delirium tremens may not be saturated with alcohol at the time.

A. Valdes Dapena, M.D., Havana, Cuba.

ANSWER.—A recent article (Perisson, J.: Alcoolisme: Traitement des Complications Nerveuses par la Strychnine, *Union méd du Canada* **72**:317 [March] 1943) which discusses the treatment of the nervous manifestations of alcohol addiction by means of strychnine contains some startling statements: Huge doses of strychnine are given subcutaneously, the daily total used in the treatment of delirium tremens being as much as 50 mg. and the individual doses being as high as 10 mg. ($\frac{1}{6}$ grain). After two or three days the dosage may be reduced, but the treatment usually lasts from five to six weeks. Smaller doses of strychnine are used in chronic alcoholism, but about six weeks of treatment are again required. It is asserted that this treatment generally causes no untoward complications, since the alcoholic patient has a remarkable tolerance for strychnine, and that strychnine is an antidote for alcohol because it causes a functional antagonism to alcohol on the nervous centers. The article indicates, however, that strychnine has no effect in the case of a demented chronic alcoholic addict.

The rationale for this form of treatment may be questioned, since a person under the influence of alcohol will oxidize or eliminate all of his imbibed alcohol within twenty-four hours after stopping drinking. It is then no longer a question of combating the narcotic action of alcohol by strychnine. Actually there is usually a period of heightened nervous irritability following alcoholic excesses, which condition would be further aggravated by strychnine. It would be better even to give more alcohol! If the strychnine treatment should measure up to the claims made in the article cited, the good results might be due to the punitive regimen.

VITAMIN K AND PHLEBITIS IN LATE PREGNANCY

To the Editor:—A patient developed a phlebitis two weeks prior to delivery. She had been taking vitamin K for some two weeks previous to the development of the phlebitis. Could you tell me whether in a case like this vitamin K will tend to cause phlebitis?

C. N. Talley, M.D., Marlow, Okla.

ANSWER.—In therapeutic doses vitamin K has little if any effect on the coagulation of the blood of normal persons. There is no experimental or clinical evidence that the administration, even in large doses, of vitamin K is followed by phlebitis. Since thrombophlebitis is not too infrequent in pregnant women, one can state confidently that in a case like that described vitamin K would not be significant in the etiology of the phlebitis.

PAINFUL BURSAE AROUND ISCHIAL TUBEROSITY

To the Editor:—Is there any such term as "bursitis ischiogluteali"? This diagnosis was made for pain on the os pubis of one side on sitting, lasting now over some years with intermissions of months. Some years prior to the onset of pain there was prostatitis. Regular and repeated treatment was instituted and the prostate is all right now.

M.D., New York.

ANSWER.—There are several small bursal pouches in the region of the ischial tuberosity. As a result of repeated irritation and sometimes following a traumatic injury there may develop a pronounced bursal swelling with chronically thickened walls. This bursa is so placed between the ischial tuberosity and the gluteus muscle that it would seem quite correct to designate this as an ischiogluteal bursitis, although that term has not been used often enough to become generally well recognized.

ALKALIS FOR SCALDING HOGS

To the Editor:—On page 320 of the May 27, 1944 issue of The Journal there is a query regarding the use of lime in scalding hogs. In the reply it is stated that packing houses have discontinued the use of chemicals; that hogs are merely scalded in boiling water and sent through the dehairers. In this connection I want to say that alkalis still are used in all packing plants in the scalding tubs in order to cleanse the carcasses. As suggested by your inquirer, lime is used, as is also soda ash and sodium hydroxide. One authority suggests 100 pounds of pine tar, 10 pounds of caustic soda and 30 pounds of soda ash for a 3,500 gallon scalding tub. It is true, of course, that workmen do not come in contact with the scalding water except in raising the tendon of the hind shank. Scalding is not done at the boiling point as the reply suggests, but at 140-146 F. Dehairing is done with a mechanical device. Some shaving is usually necessary by hand to remove hairs which escaped the beaters.

William J. Loeffel, Lincoln, Neb.
Chairman, Animal Husbandry Department, University of Nebraska.